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DIABETES ASSOCIATED WITH HÆMOCHROMATOSIS

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TROUSSEAU early in the eighteenth century referred in his clinical lectures to an autopsy upon a diabetic having a bronzing of the face, an almost black discolouration of the penis, and a greatly enlarged and cirrhotic liver. Troisier in 1871 described a similar case under the name "Diabète sucre". Hanot and Chauffard in 1882 and Hanot with Schachman in 1886 have been given the credit by most authors for first describing the disease in their reports of two cases and naming the condition "Diabète bronzé". They believed that the diabetes was the primary manifestation and that subsequently the liver cells were stimulated to an increased production of pigment.

Many authors have since commented upon the subject, and different views have been advanced. The discussions have centered about the questions pertaining to the sequence of events in the disease. One of the important points considered was whether there were two somewhat similar bronzing diseases, one associated with cirrhosis of the liver and the other with diabetes mellitus. Much has been learned of the nature of the process in each by the many clincial and pathological studies. The pathological processes leading to a deposit of iron-containing pigment in organs, many times greater than that normally found, has been an especially difficult problem for solution, partly because the blood in which one would expect to find signs of red blood cell destruction, indicates no more than a slight anæmia.

From the Pathological Laboratories, University of Pittsburgh.
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A review of the literature concerning iron-pigment deposits, a discussion of the hypotheses of the many authors and the hope of suggesting some new ideas on the subject (besides the fact that this is but the ninth case reported in the United States), is sufficient reason for bringing forward this report.

I think it can be fairly established that there are three cardinal features of the advanced cases, namely, pigmentation of the viscera and usually of the skin, cirrhosis of the liver of a portal or atrophic type, and diabetes mellitus which dominates the clinical picture of the later stages. These clinical and pathological features constitute "bronzed diabetes".

Simple hæmochromatosis without diabetes has been described a number of times (13, Potter and Milne) and it is interesting to note that in cases so described, cirrhosis of liver and other organs were also present. A minor type of hæmochromatosis has likewise been observed in a variety of diseases in which, however, the evidence of a primary blood destruction was an outstanding feature. Some of the reported cases of simple primary hæmochromatosis show that the cause of death was occasioned by an intercurrent disease, such as typhoid fever (Opie), and tuberculous peritonitis (Sprunt). It is, therefore, possible that the fatal complication prevented the development of the typical picture of bronzed diabetes before death. However, according to the observations by Anschutz on six cases of bronzed diabetes, it has been shown that glycosuria may be a very variable sign disappearing for certain periods during the disease. Letulle reported a case in which the glycosuria was absent for two months and then reappeared. Other authors have likewise noted a varying glycosuria during treatment or just before death.

I am indebted to Drs. Nettleton and Mercur for the clinical data and for permission to report the following case.

Case History: Mr. W. M. D., aged forty-six, plumber by occupation.

Family History: Father died at the age of seventy-one of cancer of the tongue; mother died at the age of eighty-one of cerebral apoplexy. Three brothers are living and well. One brother died at the age of twenty-seven, the cause of death being unknown. Two sisters are living and well.

Personal History: He has had the usual diseases of childhood. He was a heavy drinker from about 1890 to 1900, but since 1900 he has had periods of total abstinence with an occasional spree at which time he drank large amounts of whiskey. He has suffered a good deal from digestive disturbances and first came under observation in 1902 for the relief of indigestion. He complained at that time of eructation of gas and food and of feeling tired and listless. He slept well but was tired on awakening. During this illness, he lost eighteen pounds in six months. At this time he had pain and tenderness in the epigastrium. Subsequently for a number of years he suffered from gastric and intestinal indigestion. Attacks of "grippe" were frequent, yearly from

1890 until 1897, and sometimes twice a year. He also had various so-called rheumatic affections and lumbago. In 1896 he suffered an attack of gout. In 1902, until August, 1913, he had many recurrences of hyperchlorhydria.

From the time he came under observation he was never robust. His appearance was that of a prematurely old man, his hair having turned quite gray, which, however, was a family characteristic.

Present Illness: From the time he came under observation there was no indication of renal or liver disturbance until 1912, when the urine showed a few hyaline casts and a fairly well marked reaction for indican. The specific gravity was 1025. The indican cleared up after several weeks.

In July, 1913, there was a large amount of indican, which disappeared after a prolonged treatment and rest. On August 22nd, when at least semi-weekly examinations were being made, the first appearance of glycosuria was noted. This glycosuria soon became excessive, and in December he had become bed-ridden. From the time he was bed-ridden until his death, almost daily estimations of the total percentage of sugar were made by Benedict's method. Urea was also estimated from time to time.

SUGAR ESTIMATIONS

August 22, 1913	Trace.
" 23, "	No Sugar.
" 25, "	Slight.
" 26, "	Slight.

Dr. Nettleton was out of town for a period and records were not kept of the amounts of sugar found.

December	15, 1913	3·0%	December	28, 1913	2·9%
"	16, "	4·6	"	29, "	2·7
"	17, "	4·5	"	30, "	0·2
"	18, "	3·10	"	31, "	0·3
"	19, "	3·18	January	1, 1914	0·5
"	20, "	1·9	"	2, "	2·3
"	21, "	2·2	"	3, "	7·0
"	22, "	2·1	"	4, "	1·0
"	23, "	3·1	"	5, "	2·0
"	24, "	3·1	"	6, "	2·4
"	25, "	2·9	"	7, "	2·8
"	26, "	2·6	"	8, "	2·8
"	27, "	2·8	"	9, "	0·2

At no time during the course of the diabetes mellitus was the urine sugar free, the nearest approach was on December 30th when the patient had a "green day" with much nausea and vomiting. From December 15th, the patient was on strict carbohydrate free diet.

The total quantity of urine varied from 2150–4200 c.c. until January 8th, when there was almost complete suppression until death on January 12th. Acetone and diacetic acid were present in very large quantities and were constantly observed from the early part of December. Ammonia was estimated. The minimal total was recorded on December 21st at 3·029 grammes and the maximum on January 3rd at 5·0 grammes.

The patient was poorly nourished and became greatly emaciated. At no time during the course of this disease was an enlarged liver observed and the spleen was never palpable nor enlarged on percussion. There was tenderness over the liver and in the epigastrium.

The following autopsy report is taken from the records of Professor Oskar Klotz, to whom I desire to express my thanks for the assistance rendered me during the course of the work.

AUTOPSY

The body was that of a thin and much emaciated man appearing considerably older than the stated age. The skin surfaces were quite pale and rather yellow. Post-mortem rigidity was present and there was some lividity of the dependent parts. The hair was quite white, the eyes were sunken and the tissue over the cheek bones was sparse. The neck was long and thin, and the supraclavicular fossæ were quite deep. The chest was long and narrow, while the antero-posterior diameter was shallow. The abdomen was flat. There was no evidence of œdema of any of the tissues.

Thorax: The thoracic cavities were quite clear. There was no excess fluid in either cavity and neither lung presented any adhesions. The pleural surfaces were clear, shiny, and quite pale.

Lungs: Both lungs crepitated in all their parts. The lung tissue was quite soft and there was no evidence of consolidation in any portion. Foci of tuberculosis were not evident. There was a little hypostatic congestion along the posterior border of the right lower lobe. There was relatively little anthracosis in the lung tissue. Some of the lobules were bordered by lines of black pigment.

Heart: The pericardial sac contained a small quantity of clear yellow fluid. The pericardial surfaces were clear and shiny. The heart was very flabby and moulded itself in various positions when placed upon a flat surface. Both ventricles were in partial diastole. Partially coagulated blood was present in all cavities. The heart was rather globular in shape, the apex being rounded and being formed by the lateral border of the left ventricle. The tip of the left ventricle appeared to be drawn upwards on the right side. The epicardium contained a fair amount of bright yellow fat. The heart valves were fairly normal save that there was a slight thickening of the free border of the tricuspid valve as well as some thickening of the insertion of the aortic valves. The valve leaflets, however, were free and apparently competent. There were a few fatty spots upon the posterior surfaces of the free mitral cusp. The heart muscle was light in colour and of a yellowish red appearance. The muscle tissue of all parts was extremely flabby and quite easily broken. The cut muscle was rather mottled and showed some distinct yellow areas on the cut surfaces. Some of the papillary muscles of the left ventricle showed a distinct thrush breast mottling. The coronary arteries showed some yellow plaques irregularly distributed along the main vessels. This was more prominent in the coronary. The muscle of the ventricle appeared thinner than normal and the cavity of the left ventricle was enlarged. The foramen ovale was closed.

Aorta: The base of the aorta was quite thin and elastic and showed a few fatty streaks just above the aortic ring. The aortic wall showed no sclerosis. It was observed, however, that the larger vessels arising from the abdominal aorta, and particularly the superior mesenteric and splenic artery showed considerable sclerosis and rigidity of their walls.

Abdomen: On opening the abdomen very little fat was found over the abdominal parietes. This fat was quite lobulated and of a rather dark yellow appearance. The abdominal muscles were thin and appeared atrophied. The peritoneal surfaces were all clear and there was no excess fluid in the abdomen. The coils of the small intestine were free and only slightly distended with gas. There were no peritoneal adhesions. The great omentum was very thin and contained a little fat. The transverse colon was distended with gas and formed a large V-shaped loop whose lower border reached 4 cm. below the umbilicus. The liver projected 5 cm. beyond the tip of the xyphoid but the border did not extend below the costal margin on the right side. There were no adhesions in the vicinity of the liver. The diaphragm arched to the fifth rib in the right nipple line and to the sixth rib in the left nipple line. In the vicinity of the

duodenum there were no adhesions or any evidence of an abnormal process. The stomach was quite free in its position.

Stomach and Intestines: Nothing of particular note was observed in connexion with the gastro-intestinal canal. Evidence of inflammation or bands of adhesions were wanting. The bile papillæ in the duodenum appeared normal and quite patent. There was no pathological process associated with the ampulla of Vater. The appendix showed some constriction and fibrosis in its upper one-third with slight dilation in the middle third in which an enterolith was found. There were no adhesions about the appendix.

Liver: The organ was above normal size. Both lobes were well devoloped, the left appearing larger than usual. The capsule of the liver was quite thin and transparent. Along the lower border of the left lobe the surface of the liver was rather granular. There were two vertical grooves extending over the dome of the right lobe for a distance of about 12 cm. These grooves were parallel. The liver substance was brown in colour and did not have the usual red or reddish gray appearance of liver tissue. The colour resembled that of iron rust. The cut surface of the liver was quite granular and although the liver lobules were not distinct, the markings of the portal system were more prominent on account of a glassy fibrous tissue outlining them. The liver tissue was quite firm and was not readily broken. When cut with a knife the tissue appeared tough, and the cut surface was a bright brown and quite granular. The bile channels within the liver showed nothing of note. The gall bladder contained a rather dark bile but its walls were thin and normal. The bile ducts extending to the duodenum were healthy and evidence of stone, inflammation, or tumour was wanting.

Pancreas: Measured 17 x 4 x 3 cm. The pancreas was carefully dissected out with a portion of the duodenum attached. The pancreas was of good size and showed no evidence of atrophy in the gross specimen. Over the surface of the pancreas there were seen a number of small pinhead-sized white spots, which, on close examination, were found to be fat necroses. Several of these spots were also seen within the organ. The tissue surrounding the pancreas appeared quite normal. The pancreas was quite firm and on section the lobules were unusually distinct. The lobules were separated by definite and prominent fibrous tissue trabeculæ. This fibrosis was diffuse and not isolated to any particular region of the organ. The colour of the pancreas was striking and resembled that previously noted in the liver. It was of a decided bright brown or rusty character. The pancreatic ducts were not dilated and there was no evidence of obstruction or other pathological change in these passages. Some of the lymph glands in the vicinity of the pancreas were slightly pigmented while other lymph glands found near the head of the pancreas showed a very decided rusty colour. The glands though a little enlarged, showed no macroscopic evidence of fibrosis.

Spleen: The spleen was about normal in size. The capsule was thin and somewhat wrinkled. The tissue felt rather flabby and on section the organ was quite dark with occasional rusty areas. The Malpighian bodies were visible, the pulp substance was not easily broken and there was no evidence of definite fibrosis to the naked eye.

Left Kidney: The kidney was considerably larger than normal. The posterior border was rounded and of a hog-back character. The capsule was quite thin and peeled easily. The outer surface of the kidney was very pale, and rather grayish white. On section the cortex and medulla were sharply demarcated. The cortex was quite wide and of light colour and showed a rather granular appearance with streakings of red and gray. Many of the glomeruli were visible as congested dots. The pelvis and ureter were without change.

Right Kidney: The organ was similar to that of the left showing general enlargement and the light colour of the cortex. The cortex appeared wider than usual and showed similar streakings as in the left.

Adrenals: Both adrenals were of normal size. The cortex was thin and of a bright yellow colour. The medulla was soft and dark. In the medulla the tissue had a rather rusty brown apearance. The medulla was so soft that it was readily broken during removal.

Thyroid Gland: The thyroid was small, both lobes being smaller than normal. The tissue was of a dark meaty character and showed relatively little colloid. There was no evidence of fibrosis.

Anatomical Diagnosis: (Bronzed diabetes): fibrosis of pancreas; fat necrosis of pancreas; hæmochromatosis of liver, pancreas, heart, spleen, adrenal, thyroid and lymph glands, fatty degeneration of heart; brown atrophy of heart; dilatation of heart (right and left ventricles); peripheral arteriocslerosis; portal cirrhosis of liver; chronic parenchymatous nephritis.

A brief review of the outstanding points in the case both from the clinical and pathological side would indicate the following conditions. The patient was an adult male forty-six years of age; he was a plumber by occupation, and had been a heavy whiskey drinker. From 1902 until his death he suffered many gastro-intestinal disturbances and loss of weight. There was pain and tenderness in the epigastrium, but the liver was not obviously enlarged. The spleen was not palpable. The patient yearly suffered attacks of grippe and had numerous attacks of neuralgia, rheumatism, and lumbago. On August 22nd, 1913, there was found a trace of sugar in the urine which soon became excessive and the patient rapidly weakened. Acetone and diacetic acid were found in December, 1913, and the patient died in semi-coma with a terminal decrease in percentage of sugar and almost suppression of urine on January 12th, 1914. At no time was the urine sugar free. At autopsy there was found hæmochromatosis of liver, heart, spleen, adrenal, thyroid and lymph glands; portal cirrhosis of liver and fibrosis and fat necrosis of the pancreas. The pathological findings, therefore, were typical of the so-called bronzed diabetes.

Portions of different organs were fixed in Zenker's solution and in formalin for microscopical study. Microscopic sections were by the paraffine method and stained with eosin and methylene blue, hæmatoxylin and eosin Van Gieson's method and by lithium carmine and picric acid. Other special connective tissue stains were used. For iron pigment, we found that Perl's method was quite unsatisfactory. Nishimura's modification of Perl's method was substituted and our results show that this procedure is much superior for the demonstration of iron in tissues. Briefly Nishimura's test for iron pigment is as follows: formalin fixed sections are immersed in a strong solution of ammonium sulphide for one hour. Washed thoroughly in distilled water. The sections are then placed in a mixture of 2 per cent. potassium ferrocyanide and 1 per cent. hydrochloric acid for twenty minutes. Finally place the sections in 0·5 per cent. hydrochloric acid until blue (twenty minutes to one hour). Wash in water. Counterstain with hæmatoxylin and eosin or lithium carmine differentiated by picric acid and mount in balsam.

MICROSCOPICAL

Liver: The sections of the liver showed the well preserved lobules or aggregations of lobules distinctly defined by an excess amount of connective tissue in the periphery. However, a very striking feature was the presence of a large quantity of golden yellow

pigment, as fine granules or in coarse masses in all portions of the liver. This pigment was present within the lobules and was found within the liver cells as well as in the interstitial tissue. The amount of pigment within the liver cells varied from a fine sprinkling of a few small yellow granules to a crowded condition in which the substance of the cell could not be recognized. However, there appeared to be a tendency to a peripheral arrangement of the pigment in the cell. The lining cells of the bile capillaries and large bile ducts also contained the pigment.

The interstitial tissue of the portal systems was markedly increased. The greatest amount of pigment was in the periphery of the lobules in the area occupied by the portal cirrhosis. In so far as the liver parenchyma itself was concerned there was more pigment in the central portion of the lobule than in the peripheral parts. In the sinusoids a little free pigment was noted. Kupffer's cells were well filled with pigment granules. One would be led to infer that a part, at least, of the pigment present in the fibrous tissues of the portal areas had accumulated as a result of the death of some of the liver cells. In the muscle fibres of the walls of the blood vessels, in the endothelial cells of the vessels and of the perivascular lymph spaces a moderate amount of pigment was demonstrated.

Throughout the section the central portion of the liver lobule showed an adenomatous hyperplasia. These areas were small, round, and contained but a slight amount of pigment.

Sections stained with sudan showed only occasional fat droplets within the liver cells. There was no evidence of a fatty degeneration. Nishimura modification of Perl's test showed a prussian blue colour in the pigment throughout the section.

The areas of fibrosis showed a mature connective tissue with but slight progressive reaction in which lymphocytes were found. The fibrosis was distributed in a manner parallel to the direction of the vessels in the portal system. In part, it appeared that the deposit of pigment in these areas was within lymphatic spaces and at times within spindle-shaped fibroblastic cells. The fibrosis was not arranged concentrically about the pigment masses. Many pseudobile ducts were noted within this new connective tissue.

Pancreas; The lobules of the pancreas were well retained and separated from each other by strands of connective tissue, which, in places, was in excess. It cannot be said, however, that the excess of fibrous tissue was particularly of an interlobular type. More marked evidences of fibrosis were present within the lobules. There was no lymphatic infiltration in the fibrosed areas. In these situations curious patches of connective tissue occupied each lobule and pervaded the surrounding tissues in a stellate manner. These areas of fibrosis were also the site of an accumulation of a rusty yellow pigment. This pigment was found within the glandular cells of the neighboring alveoli as well as in the clefts of the mature connective tissue. Nearly every secreting cell of the pancreas contained pigment in varying amounts, more marked in the periphery of the lobule.

The pancreatic ducts showed no evidence of dilatation. It was noted that the epithelial lining of these structures was for the most part wanting or present in accumulated debris. These cells were not pigmented.

The islands of Langerhans were almost entirely obliterated. A few partially preserved islands were found. The majority of them were involved in fibrosis showing much capsular thickening and some hyaline change of the fibrous tissue. There was some pigmentation of the islands.

Several areas of fat necrosis were found in frozen sections. These areas were quite apart from the tissue involved in fibrosis or pigment deposit. A slight infiltration by lymphoid cells was seen about some of these areas of necrosis.

Lymph Gland: (Near Head of Pancreas): This gland showed quite a remarkable appearance. The whole structure with its capsule was permeated by a rusty yellow pigment which was deposited in coarse granules of irregular shape. Some of the larger pigment masses showed a granular centre with a homogeneous laminated outer struc-

ture. The pigment was present within some endothelial cells, but for the most part, it appeared to lie in the clefts of a new formed connective tissue.

The gland had lost its normal architecture and the lymph follicles had disappeared. In their place a connective tissue permeated the entire structure. The older areas of fibrosis were of a hyaline character. The lymph sinuses were quite patent and contained cells filled with pigment. On the other hand, the large lymph channels showed the presence of precipitated albumen while free pigment and pigmented cells were entirely wanting in them.

Rather curious structures were found in various portions of the lymph glands. These consisted of jointed strands showing branches and looking not unlike coarse mycelial threads of some moulds. These structures did not stain well with hæmatoxylin, and were Gram negative. Commonly they were grouped together and fibrosis was usually evident in their vicinity.

Sections of the lymph gland when treated with Nishimura's method gave a marked iron reaction. The mycelial like strands also took on the prussian blue colour.

Intestine: (*Duodenum*): Sections of the duodenum showed a normal looking structure. There was no evidence of inflammation. In the mucosal folds a slight amount of a yellowish iron-containing pigment was seen in the interstitial tissue. The epithelial cells did not contain pigment, nor was there any of it present in the deeper structures of the bowel wall.

Heart: The heart muscle was very pale and the fibres were quite narrow. Fragmentation and segmentation of the muscle fibres were evident in all portions of the tissue examined. There was no evidence of an inflammatory reaction or of old fibrosis. The arteries in the muscle tissue showed slight sclerosis. On the other hand, the muscle fibres were loaded with a brown pigment which had accumulated within their substance. This pigment was well retained even after alcohol treatment. This pigment was particularly evident in the vicinity of the nuclei and was arranged in a peculiar wedge-shaped manner towards the ends of the fibres.

Besides this another form of pigment was present in the myocardium. This was observed in the interstitial tissue between the muscle fibres. In the vicinity of the small arterioles a number of oval perithelial cells were not uncommonly seen containing much of this pigment. The pigment was much coarser and darker than that within the muscle fibres. With the test for iron, two pigments were demonstrated. One gave a positive reaction, the other was negative. The latter was deposited in the muscle fibres and corresponded to the nature and distribution of the pigment of the brown atrophy. All of the remaining pigment both within the muscle as well as in the interstitial tissue was iron-containing.

Adenal: The adrenal cortex contained very little fat. The inner zone of the cortex stained poorly and the arrangement of the cells was not as regular as usually found. The pigmented zone of the medulla was well marked. There was no evidence of an inflammatory infiltration. In the outer zone of the cortex, close beneath the capsule were found a number of patches of pigment deposit. These consisted of a brownish yellow coarse and granular pigment. The deposits were within the cells of the adrenal columns. In some places an excess amount of fibrous tissue invaded the cortex from the capsule. The pigment deposit in the outer portion of the cortex was quite distinct from the pigmented cells of the medulla. The iron reaction showed all of the pigment, except that in the medulla, to be iron-containing.

Thyroid: The section of the thyroid showed a rather congested tissue in which the alveolar spaces were small. For the most part, the alveoli consisted of small gland-like structures devoid of lumina. Colloid was present only in slight amounts. The alveoli were not enlarged, and it was only seldom that the epithelial lining was thrown into folds. The epithelial cells were, for the most part, cubical. Many of the alveoli contained a fine pink-staining granular material.

An interesting feature was the presence of a granular yellow pigment similar to that previously described, which was present in the epithelial cells lining the alveoli. In the interstitial tissue which was slightly increased in amount there was moderate

pigmentation. The pigment lay in fibrous tissue cells. Again some slight pigmentation was noted in the endothelial cells lining the perivascular lymph spaces. Free pigment in the alveoli was only occasionally seen. There were, however, a few masses of desquamated epithelial cells with pigment lying in the lumina of the glands. This pigment gave a positive iron reaction.

Spleen: The Malpighian bodies were well defined. The central arteries showed some hyaline degeneration of their walls. The pulp substance was quite congested and in the walls of the sinuses were irregular deposits of pigment which had been phagocyted by the large endothelial cells. There was some evidence of fibrosis, but it did not appear that the tissues of this organ were particularly active in the process of regeneration or destruction of red blood cells. In the trabeculæ there were some iron deposits, the pigment being held in connective tissue cells. Likewise some granules of pigment were noted in the muscle cells of the large vessels. The pigment gave a positive iron reaction.

Kidney: There was considerable change in the cortex of the kidney. For the most part, this change was in the parenchymatous portion, there being little or no reaction in the interstitial tissue. The glomeruli were large and their capsules widely dilated, with, in many instances, a vacant space between them and the glomerulous. The glomerular capsule was not thickened. The convoluted tubules were large, the epithelium stained poorly, and the individual cells were of irregular size and shape. Many of these tubules contained a debris. A number of loops of Henle were found to contain a slight amount of yellow granular pigment. The amount of this pigment was relatively small. It was absent from the convoluted tubules and from the glomeruli. The sudan stained specimens showed an unusual amount of a fatty degeneration of all the tubules of the cortex. Likewise a considerable amount of fat was present in the collecting tubules of the medulla. In the cortex the fat was present at the base of the epithelial cells and appeared in small clusters of yellow globules. The stained tubules were sharply outlined by the amount of fat present in the peripheral portion.

The diabetes in the case reported was of very severe character, the process lasting from August 22nd, 1913, to January 12th, 1914. It was associated with the fibrosis of the pancreas and islands of Langerhans. The fibrosis in the liver and elsewhere could not have resulted in such a short period as indicated by the diabetes. Acetone and diacetic acid appeared early in the diabetes and the patient died in mild coma. Death in other cases usually occurred within a year or very little over.

From the literature of this very interesting pathological process, one can classify the views of the different authors on the etiology of bronzed diabetes into five large groups. (1) Many regard a primary blood destruction as the cardinal factor in the production of pigmentation and fibrosis; (2) another group of observers take the opposite point of view and lay no stress upon changes going on in the blood, but believe that there is a retention of the normal pigments; (3) others lay stress upon the abnormal metabolism of the cells, (a) disturbed chromogenic metabolism, (b) autolysis of liver cells; (4) some regard the condition as a form of diabetes mellitus in which the pigmentation is an incidental and secondary occurrence; and (5) many workers believe that there

may be a concomitant pigmentation and cirrhosis of the pancreas. These we will discuss in order.

Primary blood destruction or intravascular alteration of hæmoglobin with the production of pigment deposits as the basis for the sequence of events in the disease was first discussed by von Recklinghausen in 1889. He described hæmofuscin as a pale yellow non-iron-containing pigment in smooth muscle cells of stomach, intestine, blood vessels and lymphatics, and occasionally in the bladder, ureter and vas deferens. He also noted it in the connective tissue cells of Glisson's capsule, splenic trabeculæ, adrenal and the sheaths of blood vessels. In the twelve cases studied by von Recklinghausen a local and general pigmentation of the organs were observed. To this pathological condition he gave the name, hæmochromatosis. He claimed that the pigment was derived from the blood.

Processes of active blood destruction have been found in the majority of the cases of hæmochromatosis. Hæmorrhage was noted in some. Purpura was reported in four cases by Opie and recurrent purpura was observed in a case by Anschutz. Hindenlang described a case associated with morbus masulous Werlhoffi. Hintz reported two cases having hæmorrhagic pericarditis and peritonitis and one case with subcutaneous hæmorrhages. Quincke and Tillmans have reported large extravasations of blood in various tissues. Buss reported cases with hæmorrhagic pleurisy, peritonitis and pachymeningitis. Abbott and Hintz have noted chronic intestinal disease. Potter and Milne observed the presence of tuberculosis and sepsis. Sprunt had two cases with a history of dysentery. Malaria has been noted by Osler and Rolleston. Skin lesions with focal hæmorrhages have also been frequently described. Futcher had one case having a papulo-squamous eruption over the legs and one with a red eruption over the chest a week before death. Osler noted purpura and urticaria over the legs in one case and erythma nodosum in the other. Parker's case had a chronic varicose ulceration of the leg.

Anæmia was described in a case showing widespread pigmentation in the liver, spleen, and pancreas by Quincke. However, this is the only case in which a true anæmia has been described. Sprunt says in his cases the average of four counts in three cases was 4,709,000 red cells and hæmoglobin of 90 per cent. Jeanselme reported a count of 3,379,000 and later 3,308,000 red cells shortly before death, but did not see any nucleated cells. Futcher in two cases reported counts of 4,800,000 and 5,304,000 red blood

cells and hæmoglobin 87 and 95 per cent. respectively. Osler's case showed an increase in red blood cells. Ridder's case showed 4,400,000 red blood cells as the lowest count. Differential counts of the white cells have always been normal. Lipæmia has been noted. No unusual blood cells have been reported by any of the authors.

Potter and Milne suggest that an excessive blood destruction must have occurred in some cases as the accumulation of pigment was enormous and occurred within a short period of time. They note, however, that generally speaking the destruction of blood must be slow to permit a more or less complete regeneration as indicated in high blood counts commonly found.

M. E. Abbott who studied the only complete case of hæmochromatosis reported in a woman, believed that simple blood destruction in itself did not cause hæmochromatosis, but that another factor such as degeneration of cells of certain organs whereby they were unable to throw off the pigment reaching them, must be associated with it. She believed that with the disintegration of these cells the liberated pigment induced an interstitial inflammation and cirrhosis of these organs. The whole process was supposed to have some active cause leading alike to blood destruction and cell degeneration, such as a bacterial infection with chronic suppuration or chronic intestinal disturbance. Adami believed that a true destruction of red blood cells occurs over a long period of time and also suggests that it is the result of bacterial invasion. Abbott believed that the pigment formation occurred before the cirrhosis, because evidences of broken down heavily pigmented liver cells lying in new formed connective tissue areas were found. Opie, Anschutz, Hintz, and Kretz have all made similar observations and draw the same conclusions. Abbott studied forty-one other cases in which a golden brown pigment could be demonstrated microscopically in the liver cells. Cases of pernicious anæmia were not included in this series. In four of these cases the presence of hæmosiderin was demonstrated. A history of localized blood disintegration or some chronic intestinal disturbance was revealed in all. Abbott also suggested that both hæmosiderin and hæmofuscin contain iron.

In his conclusions on a series of twenty-four cases Anschutz particularly brought out the fact that the blood destruction and the blood formation did not keep pace with each other, with the result of enormous deposits of pigment in the tissues. At the same time he noted a diseased condition of the glandular organs, which

under some mysterious influence took up and bound large amounts of the products of blood destruction. In the organs in which evidence of degeneration was more pronounced, a reactive inflammation resulted in connective tissue growth. Diabetes, he claimed, is the result of these extensive lesions involving the pancreas.

Rossle held that the blood destruction was secondary to capillaritis with hæmorrhage and that the abnormal hæmolytic and phagocytic activity of the liver cells accounted for the marked pigmentation of that organ. Pigment, resulting from destruction of red blood cells in liver cells, was later disseminated by the blood stream through the whole body. He believed that after this stage there is rapid regeneration of blood. Potter and Milne substantiate the finding of phagocytosis of red cells by the liver cells under pathological conditions, but, at the same time, believe that these liver cells are degenerated. They ask why should spontaneous phagocytic activity on the part of liver cells for red blood cells alone occur and if this is the cause of hæmachromatosis, why is the condition so rarely seen clinically.

Marie believed that there was some primary cause for the dissolution of hæmaglobin in the blood and tissues as shown by the presence of pigment in the various body cells. He advanced the idea that this pigment in the cells was laid down by the cell as a protection against the irritating substance destroying the hæmoglobin. This pigment in turn causes degeneration and destruction of these cells with supplementary elimination by way of lymphatics and overloading of the lymph nodes and production of inflammation and fibrosis. He concluded that bronzed diabetes was neither an ordinary clinical nor pathological diabetes, but rather a clinical entity in itself.

Achard, Dutournier and Jeanselme reiterate the statements of Marie, and as expressed by Futcher, they presuppose an unknown type of blood destruction. Opie expresses the opinion that under the conditions of the disease there is an active hæmolytic and toxic substance in the blood which transforms hæmoglobin into hæmosiderin. Buss studied one case and come to the conclusion that primary blood dissolution was the ætiological factor of the fibrosis and diabetes.

Hunter in 1888 was the first to contest blood destruction as primary in the process. He showed that hæmorrhage into the skin would only cause a local deposit of iron-containing pigment and no accumulation elsewhere. Cases of epistaxis and chronic suppuration were studied by Abbott and a case of purpura by Zaleski,

without finding any deposit of iron pigment. Futcher did not find any pigment deposit in a case of purpura and Hiss and Zurhelle had similar negative findings in a case of hæmoglobinuria.

Kretz studied cirrhosis of the liver and in fourteen of twenty-six cases he found there was hæmosiderin in the liver. He concluded that the same toxic substance caused degeneration of the liver cells and injured the red blood cells. Abbott also found hæmosiderin in six out of sixteen cases of cirrhosis of the liver and concluded that the two factors, liver disease and blood cell destruction were essential. She noted œsophageal hæmorrhage and other hæmorrhages in these cases of cirrhosis. However, Marie regarded the tendency to hæmorrhage in hæmochromatosis as a secondary manifestation. Potter and Milne believed that these hæmorrhages found in hæmochromatosis were no more than those seen in any ordinary cirrhosis of the liver. Anæmia is usually slight or absent and evidence of blood destruction was not found by them.

Sprunt noted that the pigment deposit varying considerably in quantity, exceeded that in pernicious anæmia. He further observed that the bone marrow was not actively hæmopœtic and in the study of three cases but one showed slight hyperplasia. He concluded that the findings were insufficient to signify blood destruction since in hæmochromatosis other pigments are found having no relation to hæmoglobin. Elmer studied hæmochromatosis and found no anæmia, hæmolysis nor hyperplastic bone-marrow.

French found no free pigment in the blood, but all of it was intracellular, and on this account concluded that the pigment formation did not occur in the blood stream but in the living cells.

Experiments have rather proved against an abnormal blood destruction as the primary cause of hæmosiderosis. Auscher and Lapique injected blood into the peritoneal cavity and found iron pigment in the spleen but not in the liver. He considered that he had produced hæmochromatosis but no connective tissue increase or inflammatory reaction in the tissues. Biondi gave toluylendiamin by mouth and subcutaneously to produce blood destruction. He produced anæmia, jaundice, hæmoglobinuria, pigmentation of liver, spleen, bone-marrow, lymph nodes and occasionally kidney. His conclusions were that this hæmoglobinæmia which he had produced caused the liver cells to increase their secretion of bile, even to such an extent as to cause jaundice without obstruction of the bile passages. The other part of the hæmoglobin molecule,

the iron-containing one, was taken up by leucocytes and distributed to other organs. He only found hæmosiderin in degenerated liver cells, and inferred that the diseased liver cells lost their normal capacity of ridding themselves of iron-containing pigment and that siderosis was but the expression of this fact. Sprunt discussed this experiment and concluded as there was no cirrhosis that it had no bearing upon the case in point.

Rolleston suggested that since in chronic hæmolytic jaundice there is destruction of red blood cells, the absence of jaundice in hæmochromatosis would argue against the existence of active hæmolysis.

The theory that the pigment under discussion is produced in the various parenchymatous cells or by some chemical change in the chromogenic constituents of cells was advanced by Mosse in 1894. He held that pigment was formed universally, even in the deeper cells of the Malpighian layer of the skin and was not transferred from other places of formation. The pigment accumulation in the liver is in proportion to the specialization of these cells to the chromogenic function and to the volume of blood which transverses it. He also believed that hyperglycæmia altered the blood before this specialization. On the other hand Macallum stated that iron is found in all nuclei in amounts proportionate to the chromatin present in the cytoplasm of all gland cells producing ferments. Opie suggested that the same condition which causes the deposit of pigment favours chromogenic metabolism, especially in the liver, which is present under normal conditions. This chromogenic metabolism may be the cause of pigment deposits in other organs, or it may be that the iron-containing derivatives of hæmoglobin are not eliminated by the liver and are left in the blood.

Parker believed that there was no unusual blood destruction but that there was an accumulation and lack of elimination of the normal end products. The hæmoglobin lies where it falls and undergoes some chemical change. He concludes that some toxic agent causes degeneration and chronic inflammatory changes in the liver and pancreas. Heller and Martineck are of the same opinion. Parker refers to Croftan's experiments and states that when the pancreatic lesion is of sufficient intensity there is insufficient glycolytic ferment produced by the islands of Langerhans, to act with the muscle ferment in the oxidation processes of carbohydrate metabolism. The glycogen then is not stored and a hyperglycæmia results, which in turn, causes the changes of hæmoglobin into hæmosiderin, instead of bile pigment. He also pointed out

that if the liver be normal the pigment is removed and the case is one of frank diabetes, whereas if the liver is cirrhotic the pigment is not eliminated and accumulates with hæmochromatosis as an end result.

Recently Garrod, Gaskell, Sladden, Wallis and Vaile together have reported a case in which they favour the idea of defective elimination because they did not find iron in the bile, fæces, or urine. They found that there was an increased amount of iron in the blood (from 0·042 to 0·048 and 0·056 per cent.). They proved pancreatic insufficiency the cause of the diabetes. Of note is that they also found hæmosiderin in the distal convoluted and collecting tubular renal epithelium in bronzed diabetes and in the proximal convoluted tubules in pernicious anæmia. They brought out the old theory of resorption of certain substances by the collecting tubules, in explanation of hæmosiderosis in bronzed diabetes as a result of defective elimination.

Brown attempted to prove that the process of pigmentation is not hæmolysis but autolysis. He placed rabbit's liver in moist aseptic chambers and incubated at 37°C. The results of his experiments showed an increase in the iron-containing pigment near the exposed or outer surfaces, and from this he concluded that hæmosiderin was the oxidation product of hæmoglobin due to enzyme action. Along these lines Sprunt suggested a widespread parenchymatous degeneration of a specific nature affecting many organs and leading to the deposit of a variety of pigments depending upon the chemical process in the cells. Moreover, he found little justification for the theory of primary blood dyscrasia since no anæmia was present and the bone marrow was negative. The pigment also exceeds that found in pernicious anæmia and he holds that it is a different chemical nature. He concludes that hæmochromatosis is a metabolic disease implicating many tissues and manifested by changes in the chromogenic groups or protein molecules of cells with the deposit of pigment. As a result of pigment accumulation in the interstitial tissues there occurs a reactive inflammation with fibrosis in various organs.

Sprunt, Colwell and Hagan supporting the theory of autolysis and following Brown's experiment placed sections of the perfused liver of a rabbit into aseptic moist chambers and incubated at 37°C., while others were exposed to sunlight. They did not get constant results. From their observations they have shown that iron-containing and other pigments may be found during autolysis of the parenchyma independent of hæmoglobin and hence are

derived from the protein constituents of cells. Gortner has demonstrated that the pigmentation of the integuments of larva to be the result of the interaction of oxydase and chromogen. The chromogen is present in very small quantities and is probably secreted only as needed for pigmentation while oxydase is present in relatively large amounts. The pigmentation produced by autolysis can, therefore, be explained by the action of oxydases on the chromogenic radical of the protein molecule. It is known that excessive chromogenic material is present in peculiar degenerations of the cell protoplasm and when acted upon by the ever present oxydase is precipitated a pigment.

Hess and Zurhelle believed that increased blood destruction is not necessary but that the abnormal retention of pigment is sufficient to explain this condition. They estimated 38·7 gm. of iron in the liver of their case which is one hundred times that of normal liver, fifteen times that of hæmoglobin and ten times that of the whole body; and in the pancreas, heart, and lymph nodes, 12 gm., totalling about 50 gm. in the body. They estimated the whole amount in normal blood at 2·4 gm. Since about one tenth of the red blood cells are dissolved in one day thus liberating 0·24 gm. iron and if little were lost by excretion it would require about seven months to produce the amount found in their case. This would be a very short time for this disease to develop.

Similar large amounts of iron have been isolated from the liver by Anschutz, Muir, and Dunn. The latter authors estimate that the total quantity in the body in bronzed diabetes is well over 40 gm., while under normal conditions there is not over 5 gm. They point out that the food is the ultimate source of the iron of the body and that the daily intake cannot be more than 30 mgm. If the source of the iron deposits were alone from the food, it would take some three years to accumulate the quantity found in the tissues in bronzed diabetes. As Garrod was unable to find any iron in the urine, bile, or fæces in bronzed diabetes, it would appear that there was an unusual retention of these substances by the tissues. In marked contrast are the results of iron deposit in pernicious anæmia where the various excreta contain iron bearing subtances, while the remaining surplus accumulates in the tissue. Under experimental conditions this tissue accumulation is only transient in that with the removal of the blood destruction the pigment substances soon leave the tissues. There is much to be said for the contention that bronzed diabetes is in great part determined through an unusual iron retention of the tissues. Muir and Dunn

suggest that many tissues have an unusual affinity for iron in this disease.

In a subsequent series of experiments the authors demonstrated that iron is rapidly stored in the liver and other organs during an experimental anæmia. The iron in the liver and kidneys is, under these conditions, increased five fold and in the spleen three fold. Nearly all the iron attending the destruction of blood accumulates in the liver, spleen, and kidneys. A relatively small amount escapes in the urine. It was further found that the iron stored in various organs again disappears with the regeneration of blood and probably has been utilized in the process of blood formation.

Since Hanot's report in 1882, most of the French authors have held that diabetes was the primary condition leading to blood alteration and destruction. In 1882 Hanot and Chauffard found that pigment hypergenesis of the liver cells was due to nutritional disturbance brought on by an associated diabetic endarteritis. They believed that the pigment was distributed from the liver as emboli. Letulle suggested hyperglycæmia as the cause of the blood destruction and said that the pigment was formed everywhere and accumulated in situ, especially in dead liver cells. He discredited Hanot's idea of hypergenesis particularly as he noted degeneration and pigmentation of heart cells. This observation led him also to believe that the embolic theory of Hanot's was not tenable. Brault and Galliard laid stress on diabetes as the etiological factor in the pigmentation because it seemed that in this disease the hæmoglobin is rendered incapable of transformation into normal bile pigments. They considered diabetes and liver cirrhosis concomitant, in which the degenerated liver cannot elaborate and utilize the altered blood pigments. Hernandez thought that the dissolution of hæmoglobin was due to the diabetes and that the pigments deposited in the cells of the liver altered their nutrition and finally caused their destruction. He held that the pigment could be carried by the lymphatics. Mosse believed that hyperglycæmia caused the dissolution of hæmoglobin and that the pigment deposit in the liver was in proportion to the specialization of the chromogenic function of liver cells and also to the volume of blood passing through the organ. De Massary and Potier confirm this.

Rendu and de Massary advance the hypothesis that pigment is deposited in various cells by the abnormal action of tissues on the hæmoglobin. This altered metabolism is but the manifestation of a general cachexia caused by diabetes associated with cirrhosis of the liver. Naunyn ascribed the diabetes in some cases of hæmo-

chromatosis to cirrhosis of the liver. Potter and Milne claim that in 2 per cent. of cirrhosis of the liver there is diabetes while Palma and Van Noorden hold diabetes and cirrhosis so rarely concomitant that it is only a coincidence. Simmonds reports cirrhosis of the liver in 5 per cent. of diabetes. Futcher noted bronzing in 2 per cent. of 256 cases of diabetes.

Buss found that glycæmia may result in incomplete oxidation of altered hæmoglobin. Parker has questioned the relation of diabetes to pigmentation. In ordinary diabetes there is no accumulation of iron pigment as indicated in the studies of Zaleski, Kretz, Hanot, and Hanseman.

Another group consisting mostly of German authors have considered cirrhosis of the liver and diabetes concomitant but that the diabetes comes on when interstitial fibrosis of the pancreas has reached an advanced stage. This view based upon the clinical finding of diabetes as a terminal condition is at present held by most authors. The diabetes is often very severe after the patient has shown pigmentation of the skin. The patient usually lives but a year or a little more and dies in diabetic coma.

The true sequence of events as believed by Marie, Acard, Dutournier, Jeanselme, Anschutz, and Opie is that blood destruction or altered chromogenic function with or without concomitant degeneration of liver and pancreas, or with subsequent interstitial inflammation and fibrosis of the liver and pancreas, is the first stage of the disease or simple hæmochromatosis, and that when the chronic intra-acinar pancreatitis has reached a sufficient degree of severity the characteristic symptoms of diabetes develop. Potter and Milne hold that in every case of liver cirrhosis hæmosiderin may be found in some of the organs and that hæmochromatosis is but an exaggeration of this. The cirrhosis is primary and is the result of the same toxic agent which produces the blood destruction. The pancreas may be damaged as a sequel to or coincident with the cirrhosis of the liver, or on the other hand, it may be due to a catarrhal inflammation of the secretory channels of pancreas with secondary atrophy and sclerosis.

In our own case no blood counts were recorded which would indicate the degree of blood destruction, but the patient was observed to be quite anæmic for a long time. He had, however, never had any gross hæmorrhage. One point of note is that our patient had been a plumber the greater part of his life and might have suffered, although never recognized, lead poisoning with its associated blood destruction.

We consider blood destruction to some degree a factor in the production of hæmochromatosis, pointing out that blood counts had only been taken during the later stages of the disease in other reports. I have noted in a case of primary carcinoma and cirrhosis of the liver as well as in several cases of pernicious anæmia a considerable pigmentation of the liver and spleen. The distribution of pigment in these cases is both in Kupffer's cells and liver cells, but in considerably smaller amounts than in bronzed diabetes. I have also noted in a case, twice having chronic lead poisoning, an iron-containing pigment in the Kupffer and parenchyma cells of liver. Ophuls in his reports on chronic nephritis by lead poisoning has likewise noted pigment deposits. A case of advanced tuberculosis with marked anæmia reported by Roque, Chalier, and Josserand showed pigment deposits especially in the liver and spleen, an advanced stage of hæmochromatosis.

The small amount of iron-containing pigment in the kidney was remarkable in comparison to the deposit found in other organs. In our analysis of tissues in pernicious anæmia a much larger quantity was found in the kidney. These results are parallel to the urinary findings, where no particular pigment is observed in bronzed diabetes while a varying and even marked amount may be observed in pernicious anæmia. The difference suggests the lack of a mobile pigment in the former. It is of interest, however, that whereas in bronzed diabetes the pigment deposit in the kidney is localized to a few cells, that in the anæmias the deposits may occupy various portions of the tubules. The presence of iron-containing pigment in the fæces, in view of the liver cirrhosis and the associated portal stasis and hæmorrhage, has no renal significance.

The experiments of Auscher and Lapique, Meunier and Biondi, have shown that blood destruction caused a deposit of iron-containing pigment in varying amounts. These experiments show that some added factor must be necessary to produce fibrosis. Time may be that factor because the portal cirrhosis of the liver in bronzed diabetes is of long duration, while the experiments and the course of pernicious anæmia are usually more acute. Alcoholism or lead poisoning may also be an associated exciting factor.

In our case, pigment deposits as well as sclerosis were found in large amounts in the liver, pancreas, lymph glands about the pancreas, spleen, heart, thyroid, and adrenal. It is possible that it was present in more tissues. Others have found iron-containing pigment in Brunner's and the glands of stomach, duodenum, and

small intestine. Likewise pigment has been found in the parathyroids and the glands about the trachea, bronchi, and larynx as well as in the skin, œsophagus, aorta, submaxillary, axillary, mesentery, and mediastinal glands, in cartilage cells of trachea and costal cartilages, in the kidneys, bone marrow, and in several cases in the testes, prostate, vas deferens, seminal vesicles, and urethral epithelium.

In the case reported, definite pigmentation of the skin was not noted at autopsy, but a slight and varying pigmentation of the exposed surfaces was noted clinically. The skin pigmentation is the not uncommon clinical feature of the disease by which it is recognized during life. When present it is most marked on the exposed parts, the face, neck, back of hands, shins, in the axilla and groin and about old scars and is of a diffuse slaty blue or brownish gray colour with darker spots like freckles. No pigment is seen in the sclera or on the mucous membranes.

The distribution of the iron pigment in cells is not regular. Side by side one collection of cells may be filled with granules, while others nearby may show little or none. There is commonly no relation between the pigmented cells and the blood or lymph channels. It has been suggested that the pigment accumulates in the cells on account of an abnormal condition under which they are placed, and that cells which normally have no relation to pigment production are found to deal with this unusual product.

Of the chromogenic metabolism of cells we know but little. The accumulation of blood derivatives might result from the hæmoglobin reducing processes of the liver and heart, but this would hardly suffice to indicate the mode of deposit in the lining cells of the thyroid and pancreas. There can hardly be any doubt that there is some alteration in the chemistry or selective activities of the various cells whereby they show an abnormal property of taking up iron pigment. Whether the excretory organs themselves have an unusual ability of withholding iron from their secretions is not clear.

The pigment is not only distributed to glandular cells, but also to connective tissue, endothelial and lymphatic cells. These cells obtain their pigment directly from the blood as is indicated in the widespread and irregular distribution with no relationship to other structures. Free hæmoglobin has not been demonstrated in any of the reported cases, but this may be the result of faulty technique. The chemical tests for minute quantities of iron-

containing pigment in the blood plasma are insecure, and spectroscopic methods have as yet not been applied in these cases.

Another point of contention and cause of much discussion is the finding of the two pigments, hæmofuscin and hæmosiderin, in almost all the organs. These pigments have commonly been found side by side and have about the same morphology, the hæmofuscin being of a canary yellow, while hæmosiderin is rusty brown and usually in large coarse clusters. Many authors have used some modification of Perls' reaction, obtaining better results with the hot hydrochloric acid as suggested by Abbott. In our case the pigment did not react to the original Perls' test but showed a slight reaction when the hot hydrochloric was used. On the other hand a brilliant reaction was obtained by Nishimura's ammonium sulphide modification of Perls. It would appear from our results that possibly all of the pigment is iron-containing, but some is more closely bound and hence more difficult to demonstrate. A similar view has been expressed by Abbott, Futcher, Hiss and Zurhelle, Sprunt, and others. M. B. Schmidt points out that although the pigment fails to respond to the available tests for iron, it is not necessarily iron free and hæmofuscin may be an older stage in the chemistry of the pigment.

In our case cirrhosis of the liver was not recognized during life, the liver being slightly enlarged and there being no ascites. The spleen showed no enlargement. There were no hæmorrhages. However, there had been a long period of dyspeptic symptoms with tenderness in epigastrium, which in the absence of any lesion in the stomach and intestines may have had some association with the cirrhotic liver. The fibrosis of the liver is probably not directly due to the pigment deposited in interstices by degenerating cells. as it is not disposed around the pigment masses. This can be said only in part of the other organs because some show evidence of irritation and an enclosing fibrosis. Particularly was this true of the lymph glands.

BIBLIOGRAPHY

ABBOTT.—*Jour. of Path. and Bact. Edin.*, 1901, vii, 55.

ACHARD.—*Thèse*, Paris, 1895.

ADAMI.—*Jour. Amer. Med. Assoc.*, 1899, xxxiii, 1506.

AUSCHER and LAPIQUE.—*Compt. rend. Soc. de biol.*, 1895, 10, 402, 510; and 1898, 10, 185.

BEATTIE.—*Jour of Path. and Bact.*, 1903, ix, 117.

BRAULT and GALLIARD.—*Arch. gen. de Med.*, 1888, i, 38.

BROWN.—*Jour. Exper. Med.*, 1910, xii, 623.

BIONDI.—Ziegler's "Beitrage", 1895, xviii, 176.

CECIL.—*Jour. Exper. Med.*, 1909, xi, 275.

DE MASSARY and POTIER.—*Bull. Soc. Anat. de Paris*, 1895, lxx, 354.

FUTCHER.—*Amer. Jour. Med. Sci.*, 1907, cxxxiii, 78.

GAEBEL.—Virchow's *Archiv.*, 1894, cxxxvi, 482.

GORTNER.—*Jour. Biol. Chem.*, 1910, vii, 365.

GASKELL, SLADDEN, WALLIS, VAILE, and GARROD.—*Quart. Jour. of Med.*, 1914, vii, 129.

HANOT and CHAUFFARD.—*Rev. de Méd.* Paris, 1882, ii, 385.

HANOT and SCHACHMAN.—*Arch. de physiol. norm. et path.*, Paris, 1886, vii, 50.

HISS and ZURHELLE.—*Zeit. f. klin Med.*, 1905, lvii, 349.

HINDENLANG.—Virchow's *Archiv.*, 1880, lxxix, 492.

HINTZ.—Virchow's *Archiv.*, 1895, cxxxix, 459.

JEANSELME.—*Presse Medicale*, 1897, ii, 852.

KRETZ.—*Centralb. f. Allg. Path.*, 1897, viii, 620.

LABBE and BITH.—*Bull. de Soc. Méd. de Hop. de Paris*, 1912, xxxiii, 119.

LABBE.—*Arch. de mal. de l'appar. digest.*, Paris, 1912, xl, 403.

LETULLE.—*Soc. Méd. de Hop. de Paris*, 1885, ii, 406; and 1897, xiv, 205.

MARIE.—*Semaine Méd.*, 1895, xv, 229.

MELTZER.—*N. Y. Med. Rec.*, 1900, lvii, 43.

MUIR and DUNN.—*Jour. Path. and Bact.*, 1915, xx, 41; and 1915, xix, 226 and 417.

NAUNYN.—*Diabetes Mellitus, Wien*, 1906.

OPIE.—*Trans. of Assoc. Amer. Phys.*, 1899, xiv, 253.

Idem.—*Jour. Exper. Med.*, 1899, iv., 279.

OSLER.—*British Med. Jour.*, 1899, ii, 1595.

POTTER and MILNE.—*Amer. Jour. Med. Sci.*, 1912, cxliii, 46.

QUINCKE.—*Deutsch. Arch. f. klin. Med.*, 1880, xxvii, 260.

ROSSLE.—Ziegler's "Beitrage", 1907, xli, 181.

SCHMIDT.—Virchow's *Archiv*, 1889, cvx, 397.

SPRUNT.—*Arch. Int. Med.*, 1911, viii, 75.

SPRUNT, COLWELL, HAGAN.—*Jour. Exper. Med.*, 1912, xvi, 607.

Idem.—*Amer. Jour. Med. Sci.*, 1902, cxxiii, 662.

TROISIER.—*Bull. Soc. Anat.*, Paris, 1871, xiv, 231.

THE MODERN LABORATORY INVESTIGATION OF A NEPHRITIC

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As a preliminary to the subject proper let me point out very briefly the present day conception of the rôle played by the kidney in the animal economy. Bayliss[1] in his recent work summarizes it as, first, the removal of non-volatile products of metabolism which are useless or injurious, and second, keeping the osmotic pressure of the blood constant. This osmotic pressure is due chiefly to the salts, and, their excretion must be increased or decreased according to the amount taken in with the food, and the excretion of water adjusted according to that taken in or lost in various ways.

For over seventy years two general theories of urinary secretion have existed—that of Ludwig on the one hand, and that of Bowman-Heidenhain on the other. According to Ludwig, secretion of urine is a process of simple filtration through the epithelium of the capillary wall and of the glomerular epithelium. With it are carried sodium chloride, other inorganic salts, and urea, and during its passage down the tubules concentration occurs by loss of water to the more concentrated blood and lymph.

On the other hand Bowman and Heidenhain held the glomerular process to be a secretory act, secreting water and inorganic salts, while urea and other urinary substances were secreted by the epithelium of the tubules.

Physiologists to-day are not agreed, but it is admitted that by whatever method, water and salts leave the kidney through the glomerulus and the majority incline toward the more active secretory method of Bowman-Heidenhain. Water is again resorbed by the urinary tubule epithelium and uric acid, phosphoric acid, and foreign substances are excreted here as well.

The functionating unit then of the kidney consists of a glom-

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erulus and the tubule which drains it into the kidney pelvis. Gerrish estimates that a normal kidney contains about half a million of such units and that the tubules would extend in total length about fifteen miles.

Just as the normal heart has a great reserve of power, so the kidney possesses a great reserve of function. Indeed it has been estimated that one half of one kidney or one fourth of the total kidney substance is quite able to carry on the necessary excretion. Herein lies the explanation of the fact that a person may live with a large portion of the kidney substance diseased. Under such circumstances, however, the healthy parts functionate under increased tension and must have a perfect blood supply. Any interference with this supply, either local or general, proves immediately serious. Similarly any poison or irritant substance provides a serious menace to such a case.

The blood supply of the kidneys is large. Councilman[2] estimates that this supply may vary nineteen times as much as the average supply to other organs.

The volume of urine eliminated varies with many factors, but chiefly with the fluid ingested and the condition of the circulation. If the blood is hydræmic from ingestion or from the elimination of exudates and œdemas, this favours the condition of polyuria. Rises of blood pressure tend in a general way to increase the amount excreted and *vice versa*. Of course, here it must be remembered that the rise in blood pressure may be offset by a constriction of the renal vessels. Drugs of the caffeine group produce diuresis largely by the improvement of the circulation through the kidney and partly by direct stimulation of the renal cells. Digitalis, in addition to helping the circulation dilates the renal vessels and according to some observers has a specific action upon the kidney cells.

Having thus briefly referred to this aspect of kidney physiology, let me refer back to what is designated as the kidneys first function, i.e., the removal of the non-volatile waste products of metabolism. Since protein substances are essential constituents of all living cells, and without them vegetable as well as animal life is impossible, it necessarily follows that we cannot adequately consider disturbances of kidney function without at least some familiarity with the more outstanding phases of the metabolic processes which concern these substances.

Proteins differ from fats and carbohydrates by containing nitrogen in addition to the carbon, hydrogen, and oxygen common

to all. Generally sulphur and sometimes phosphorus are constituents. The most important element, however, is nitrogen.

Decomposition or cleavage of protein substances is brought about by hydrolysis, and this occurs in digestion by the action of the proteolytic enzymes. In this process the protein molecule is gradually broken down and less complicated aggregates first result which are known as proteoses, peptones, and peptides, and these still possess true protein characteristics. Further hydrolysis results in the transformation of these simpler protein substances into amino acids of a known chemical structure, and devoid of any protein characters. Thus from protein, of huge molecule, colloid, slightly soluble, and non-diffusible, we pass by way of proteoses, peptones, and peptides to a class of simpler crystalline substances which are for the most part readily soluble and diffusible. I shall not here enumerate the long list of these amino acids which is contained in any reference book.[3] Suffice it to say that they are most important, and are amphoteric, being able to form salts with both bases and acids.

Some of these amino acids are destroyed by intestinal bacteriæ but most of them reach the portal blood, thence through the liver to the systemic circulation where some of them are eagerly seized by the tissue cells and synthesized into the various complex proteins of the organism. Others remain in the blood and there is always a certain equilibrium between the amino acid content of tissues and blood.

In the process of tissue building the great diversity of amino acids required for different tissues leads to the rejection of some, which if not specifically required, are carried to the liver where the nitrogenous portion is converted to urea. In addition it is believed that there is a constant migration of amino acids from tissue due to disintegration of tissue proteins. Some of these are likewise in the liver converted to urea.

This conversion from amino acids to urea is carried out by:

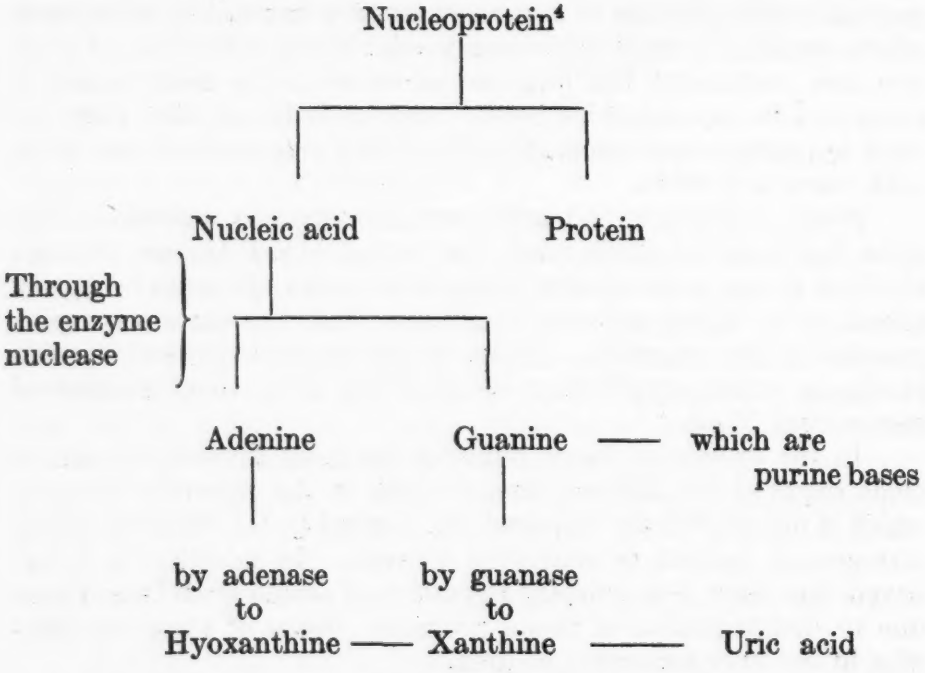
1. Deaminization, or the splitting off of ammonia.
2. This ammonia unites with CO_2 of the blood to form ammonium carbonate.
3. Which in turn is converted to ammonium carbonate,
4. And finally to urea, which is the principal end product of ordinary protein metabolism in human beings.

It is believed that other tissues of the organism besides the liver have very slight power of urea formation.

A second very important decomposition product of protein

metabolism is ammonia, which may be liberated in the intestines during digestion and thence pass to the liver where it may be converted to urea. Some of this ammonia as well as ammonia from deaminization may escape transformation into urea, in order that when excreted by the kidney later it may neutralize the sulphuric, phosphoric, and uric acids of the urine.

A third product of protein cleavage is uric acid which arises from the breaking up of nuclear material. This process may be exogenous, in the intestines due to trypsin, or endogenous in the tissues due to a similar enzyme. Foods such as pancreas, thymus, liver, kidney, and testicles are rich in nucleoproteid.



A small amount escapes conversion into uric acid and gives rise to the purine bases of the urine.

The substitution[5] of uric acid for urea as the form of nitrogenous waste in reptiles and birds is an adaptation to conserve the water of the body and fit them for a dry climate. Uric acid has very little affinity for water and is almost insoluble, and in birds urine is excreted as crystalline masses, while urea has a great affinity for water and takes a great deal of water out of the body with it while being excreted. In birds, however, the formation of uric acid is analogous to the formation of urea in man, i.e., by

a synthesis chiefly in the liver. In man, it is worthy of note, that a small part of the ingested purines are converted into uric acid later, and the remainder probably are destroyed by bacteria in the intestine or in the tissues.

Creatinine is a substance found in the blood and excreted in the human urine in amounts of 1 to 2 grams daily and is entirely independent of the protein intake. The amount is roughly proportional to the body weight—about 7–11 mgs. of creatinine nitrogen per kilo of body weight. This is termed the creatinine cœfficient.[6] It is found normally in the liver, heart, and voluntary muscle as well as in the brain, testicles, and some other organs. The antecedent state of creatinine is creatine and the muscles and some other organs including the kidney likely have the capacity of converting creatine into creatinine. Folin suggests, in view of all the known facts in reference to creatinine, that it is entirely endogenous in orgin and that it is an index of the real catabolism of the vital machinery of the body proper, in distinction from that catabolism which increases the free energy.

These then are the most important non-volatile products of metabolism which it is incumbent upon the kidney to remove, and even this brief and incomplete resumé of their origin and place in the economy of the organism may help to make clear some of the problems in dealing with our nephritics.

Turning now to the methods of attack in dealing with this subject, they naturally divide themselves into two groups: first, we may determine to what extent the kidney eliminates normal substances and also foreign substances such as drugs or dyes; and secondly, we may determine if any degree of retention of certain substances exists in the blood. The broad underlying principle of all tests then is that any depreciation of renal activity will be reflected in the urine on the one hand, and in the blood upon the other.

Let us first consider the examination of urine.

The elimination of water. The healthy kidney possesses to a marked degree the capacity of being able to adapt itself to any tendencies which are likely to alter the molecular concentration of the blood, e.g., the adding or subtracting of water from the blood. Normally water in excess is quickly eliminated by the glomerules and reabsorption in the tubules is inhibited, for, as you know, the glomerulus normally secrets a urine of low specific gravity, and the tubule absorbs water and some salts back into the blood again, thus concentrating it. If, on the other hand, the

supply of water to the body is limited, the absorptive capacity of the tubules is given full play, resulting in a urine of high specific gravity and saving considerable water to the organism. This is the diluting-concentrating power of the kidney and obviously suffers in disease of the kidney in proportion to the amount of parenchyma involved. A normal kidney, by adapting itself to changing influences, gives a very varied secretion, while a diseased one tends more to constancy and invariability.

In order to test this capacity in the kidney a provocative polyuria[7] test is used. The patient empties the bladder say, at 7.30 a.m. and drinks one pint of water, on an empty stomach, and remains in bed during the test. Then collect urine at 8.30, 9.30, 10.30, and 11.30 and note the amount and specific gravity of each. In three hours the patient should have passed at least one pint of urine. Under normal circumstances the polyuria appears in the first half hour, and reaches its maximum soon after.

To render this test more comprehensive, Hedinger and Schlayer[8] have proposed a test to determine the water, salt, and specific gravity of two-hourly specimens. Their work shows how normal and diseased kidneys respond to a reasonable amount of fluids, salt and purine. More recently Mosenthal,[9] in an admirable paper covering a study of one hundred cases, elaborates upon their method and his findings and conclusions are exceedingly instructive. I here quote freely from his article and many of these charts are from the same source. His test meal for renal function as used at John's Hopkins Hospital is here given.

NEPHRITIC TEST DIET

For..... Date.....

All food is to be salt-free from the diet kitchen.

Salt for each meal will be furnished in weighed amounts (213 gm.)

All food or fluid or salt not taken must be weighed or measured after meals and chartered in the spaces below;

Allow no food or fluid of any kind except at meal times.

Note any mishaps or irregularities that occur in giving the diet or collecting the specimens.

Breakfast, 8 a.m.:

Boiled oatmeal; 100 gms.
Sugar, 1 to 2 teaspoonfuls.
Milk, 30 c.c.
Two slices of bread (30 gms. each).
Butter, 20 gms.
Coffee, 160 c.c.
Sugar, 1 teaspoonful } 200 c.c.
Milk, 40 c.c.

Milk 200 c.c.
Water, 200 c.c.

Dinner, 12 Noon:

Meat soup, 180 c.c.
Beefsteak, 100 gms.
Potato (baked, mashed or boiled), 130 gms.
Green vegetables as desired.
Two slices of bread (30 gms. each).
Butter, 20 gms.
Tea, 180 c.c.
Sugar, 1 teaspoonful } 200 c.c.
Milk, 20 c.c.
Water, 250 c.c.
Pudding (tapioca or rice), 110 gms.

Supper, 5 p.m.:

Two eggs cooked in any style.
Two slices of bread (30 gms. each).
Butter, 20 gms.
Tea, 180 c.c.
Sugar, 1 teaspoonful } 200 c.c.
Milk, 20 c.c.
Fruit (stewed or fresh), 1 portion.
Water, 300 c.c.

8 a.m. No food or fluid is to be given during the night or until 8 o'clock the next morning (after voiding), when the regular diet is resumed. Patient is to empty bladder at 8 a.m., and at the end of each period, as indicated below. The specimens are to be collected for the following periods in properly labelled bottles, to be furnished by the chemical division of the medical clinic:

8 a.m. to 12 n.; 12 n. to 2 p.m.; 2 p.m. to 4 p.m.; 4 p.m. to 6 p.m.; 6 p.m. to 8 p.m.; 8 p.m. to 8 a.m.

Specimens are to be left in the ward until called for at 8.30 a.m. by an attendant from the chemical laboratory.

The above dietary contains 13·4 gm. N., 8·5 gm. NaCl. and 1760 c.c. of fluid and considerable purin material in meat, soup, tea, and coffee. It is in no way a specific one but merely such as may be supplied in almost any home and contains a sufficient quantity of diuretic material to make an adequate demand on the kidney to test renal function.

Patients are requested to take no solid food or fluid between meals or during the night, and each two-hour specimen is collected promptly, and the night urine secured ere breakfast is eaten.

If patients are irrational, or involuntary, piecemeal studies alone are possible, but such, repeated as occasion offers, supply much valuable data.

In a normal individual the points noted below are the important ones to observe in the response to a nephritic test meal:

1. Variations in the specific gravity of the urine—usually an average of at least ten points.

2. Balance between intake and output of salt, nitrogen, and fluids—should be approximately equal.

3. Night urine—should be of high specific gravity (above 1016), high in percentage of nitrogen (above 1 per cent.), and small in amount (400 c.c. or less) regardless of fluid ingested. This is the concentration power of the kidney.

NORMAL RESPONSE TO NEPHRITIC TEST MEAL

Time of day.	Amt.	Spec. Grav.	NaCl per cent.	NaCl Grams	Nitrogen per cent.	Nitrogen Grams.
8—10 a.m.	153 c.c.	1016				
10—12 "	156 "	1019				
12— 2 p.m.	194 "	1012				
2— 4 "	260 "	1014				
4— 6 "	114 "	1020				
6— 8 "	238 "	1010				
Total day	1115	....	....	9·36	....	7·32
Night 8—8	375	1020	....	2·36	1·23	4·61
Total 24 hours	1490	....	....	11·72	....	11·93
Intake	1760	....	....	8·5	....	13·4
Balance	+270	....	....	-3·22	....	+1·47

In disease conditions the kidney shows its dimished capacity by:

1. Fixation of concentration—or hyposthenuria, of Koranyi.

2. Some retention of one, two, or three of the following—sodium chloride, nitrogen, or water.

3. The night urine shows polyuria—an amount over 400 c.c. and not merely frequency of micturition. This is often the earliest symptom of renal disease. Lower specific gravity and lower nitrogen concentration are also frequently met. Normally, after nitrogen intake, its appearance in the urine is somewhat delayed, giving rise to disproportionately high nitrogen content in night urines over that of the day, commonly above 1 per cent.

Diseased conditions giving rise to variations from the normal findings, in addition to the nephritides, are œdema due to cardiac decompensation, severe anæmia, diabetes insipidus, conditions of back pressure on the kidney, as in hydro-nephrosis, hypertrophied prostate, and other kidney conditions such as the ascending infections.

SPECIFIC GRAVITY OF URINES COLLECTED IN TWO-HOURLY PERIODS

Case	Specific Gravity						Variation in Degrees
Normal	16	19	12	14	20	10	10
Incipient primary contracted kidney	09	14	09	10	14	06	8
Incipient primary contracted kidney	18	09	16	22	13	10	11
Advancing primary contracted kidney	18	17	13	13	13	15	5
Advancing primary contracted kidney	19	20	20	20	21	20	2
Advanced primary contracted kidney	11	11	10	11	11	11	1
Advanced primary contracted kidney	12	11	11	11	12	13	2
Advanced primary contracted kidney	10	09	10	09	09	10	1
Advanced primary contracted kidney	05	06	07	08	..	08	3
Incipient chronic diffuse nephritis	25	..	24	33	28	30	9
Incipient chronic diffuse nephritis	09	16	15	17	12	07	10
Advanced chronic diffuse nephritis	12	11	14	11	13	11	3
Secondary contracted kidney	09	10	12	10	12	10	3
Myocardial decompensation—congestion	18	20	19	18	20	21	3
Mycocardial decompensation—congestion	25	24	24	25	24	21	4
Myocardial decompensation—congestion	12	15	10	15	13	10	5
Polycystic kidney	10	10	10	11	10	10	1
Marked anæmia	10	10	10	10	10	11	1
Diabetes insipidus	04	04	06	04	04	04	2
Cystitis, pyelitis, prostate hypertrophy	10	10	10	10	11	11	1
Pyonephrosis	11	12	12	12	13	12	2

These are day urines. Noted fixed specific gravities.

CHART SHOWING (1) FIXED SPECIFIC GRAVITY, AND (2) CONSTANCY OF NOCTURNAL POLYURIA, IN A CASE OF ADVANCED CHRONIC DIFFUSE NEPHRITIS

Volume of Urine c.c.		Specific Gravity		Volume of Urine c.c.		Specific Gravity	
Day	Night	Day	Night	Day	Night	Day	Night
1390	560	12	10	1525	1090	12	11
935	710	12	11	1400	1260	11	10
1010	760	11	10	1146	1100	11	12
1122	705	10	10	1940	1060	10	09
790	790	10	10	1280	1520	10	09
908	1110	11	10	1640	1400	10	10
880	1184	11	10	1370	1370	11	10
1020	1360	12	09	1480	1480	18	18
1075	1120	11	10	1340	1680	19	17
1149	1255	10	10	1410	1340	10	10
1375	730	12	11	1480	1410	12	10
1600	1160	12	10	1184	1610	10	08

CHRONIC INTERSTITIAL NEPHRITIS

In early nephritis variations in renal function do not necessarily parallel the anatomical changes or *vice versa*, owing to the great reserve of kidney structure. If there is a large percentage of kidney tissue diseased or destroyed the remainder must obviously func-

tionate nearly up to, or quite up to, its full capacity, constantly, and hence little or no variations are possible in spite of varying demands. This gives rise to urines from hour to hour or even day to day of almost fixed characteristics, i.e., as to specific gravity, salt, and nitrogen.

Different stages are of course met, from slight nocturnal polyuria (more than 400 c.c.) with milder degrees of retention of salt and nitrogen, through various phases to the most severe cases.

These are summarized by Mosenthal as follows:

1. Nocturnal polyuria (over 400 c.c.).

2. Tendency to total polyuria (volume of urine equals or surpasses the volume of ingested fluids).

3. Fixation of specific gravity—gradually becoming more intense. Fixation at first occurs at higher levels and later at lower.

4. Fixation of two-hourly quantities, i.e., the usual polyuric response to meals is absent.

5. Night urine may drop to normal quantity but is of low specific gravity and nitrogen content.

6. Varying degrees of nitrogen and salt retention.

The accompanying tables indicate graphically the points enumerated.

EARLY HYPERTENSIVE NEPHRITIS

	Urine		Sodium Chlorid		Nitrogen	
Time of Day	c.c.	Sp. Gr.	Per cent.	Gm.	Per cent.	Gm.
8—10	465	1·009				
10—12	102	1·014				
12—12	205	1·009				
2—4	160	1·010				
4—6	116	1·014				
6—8	160	1·006				
Total Day	1,208			4·79		5·67
Night 8—8	935	1·010	0·33	3·08	0·50	4·67
Total 24 hours	2,143			7·87		10·34
Intake	1,760			7·50		13·40
Balance	−383			−0·37		+3·06

The nephritic test meal shows a tendency toward fixation of specific gravity and a distinct nocturnal polyuria in an early case of hypertensive nephritis.

REACTION TO NEPHRITIC TEST MEAL IN ADVANCED HYPERTENSIVE NEPHRITIS

Time of Day	Urine c.c.	Sp. Gr.	Sodium Chlorid Per cent.	Sodium Chlorid Gm.	Nitrogen Per cent.	Nitrogen Gm
8—10	133	1·010				
10—12	176	1·009				
12— 2	156	1·010				
2— 4	212	1·009				
4— 6	164	1·009				
6— 8	104	1·010				
Total Day	945		0·34	3·33		3·27
Night 8—8	590	1·010		2·01	0·38	2·24
Total 24 hours	1,535			5·34		5·51
Intake	1,510			5·80		2·20
Balance	−25			+0·46		+6·69

There is very marked fixation of the percentage figures for nitrogen and salt concentration and the specific gravity. There is evident nitrogen retention. The salt intake is too low to make it certain that a diminished ability to excrete salt does not exist.

EXTREME INTERSTITIAL NEPHRITIS

Time of Day	Urine c.c.	Sp. Gr.	Sodium Chlorid Per cent.	Sodium Chlorid Gm.	Nitrogen Per cent.	Nitrogen Gm.
8—10	24	1·005				
10—12	106	1·006				
12— 2	82	1·007				
2— 4	83	1·008				
4— 6	0					
6— 8	230	1·008				
Total Day	525		0·12	0·63	0·25	1·28
Night 6—8	1,140	1·007	0·12	1·37	0·20	2·27
Total 24 hours	1,665			2·00		3·55
Intake	1,850			6·00		13·00
Balance	+185			+4·00		+9·45

Note the low fixed specific gravity, the retention of salt and nitrogen, and the night urine which is increased in amount, shows a low specific gravity and a low nitrogen concentration.

RENAL CONGESTION, FROM MYOCARDIAL INSUFFICIENCY

These cases give the following characteristics due to the congestion and œdema affecting the kidney function:

1. Specific gravity fairly constant at a point about 1020.
2. Very low salt output.
3. Markedly good output of nitrogen—in contrast to that of salt.

4. An oliguria.
5. A normal night urine.

It is thus of considerable value to use a nephritic test meal to estimate roughly the degree of cardiac decompensation since the kidney is so sensitive to circulatory disturbances.

The following charts illustrate a couple of marked cases.

URINE IN MARKED CARDIAC DECOMPENSATION

Time of Day	Urine c.c.	Sp. Gr.	Sodium Chlorid Per cent.	Sodium Chlorid Gm.	Nitrogen Per cent.	Nitrogen Gm.
8—10	65	1·025				
10—12	53	1·024				
12— 2	51	1·024				
2— 4	49	1·025				
4— 6	37	1·024				
6— 8	57	1·021				
Total Day	312		0·58	1·81	1·53	4·77
Night 8—8	172	1·021	0·42	0·72	1·67	2·87
Total 24 hours	484			2·53		7·64
Intake	995			7·00		9·40
Balance	+511			+4·47		+1·76

Test meal in an individual with marked cardiac decompensation which has persisted for some time.

URINE IN EXTREME CARDIAC DECOMPENSATION

Time of Day	Urine c.c.	Sp. Gr.	Sodium Chlorid Per cent.	Sodium Chlorid Gm.	Nitrogen Per cent.	Nitrogen Gm.
8—10	61	1·018				
10—12	52	1·020				
12— 2	65	1·019				
2— 4	55	1·018				
4— 6	30	1·020				
6— 8	35	1·021				
Total Day	298			0·77		5·01
Night 8—8	275	1·021	0·31	0·85	1·85	5·07
Total 24 hours	573			1·62		10·08
Intake	570			5·00		12·00
Balance	−3			+3·38		+1·92

Note the high concentration of nitrogen as compared with the low figures for salt. There is a distinct oliguria. (The water output should be higher as general anasarca was present.)

In a combination of cardiac insufficiency and interstitial nephritis the urinary symptoms of either may predominate. The determining factor which decides the symptom type is probably whether or not the nephritis is so far advanced as to present an unchanging barrier to the influence of renal congestion.

Chronic Diffuse Nephritis

Here the response to the functional tests vary as much as do the clinical symptoms. During œdema formation there is salt and water retention, nocturnal polyuria with good nitrogen excretion. Hence the urinary output is very like that of cardiac decompensation. While œdema is being eliminated salt and water are above the intake and night polyuria is marked.

Chronic Diffuse Nephritis

	Urine		Sodium Chlorid		Nitrogen	
Time of Day	c.c.	Sp. Gr.	Per cent.	Gm.	Per cent.	Gm.
8—10	32	1·025				
10—12						
12— 2	54	1·024				
2— 4	64	1·033				
4— 6	64	1·028				
6— 8	66	1·030				
Total Day	280			0·50	1·91	5·34
Night 8—8	595	1·016		0·46	0·93	5·53
Total 24 hours	875			0·98		10·87
Intake	1,760			8·50		13·40
Balance	+885			+7·52		+2·53

Test meal in a case of chronic diffuse nephritis during the formation of œdema. The marked salt and walter retention, the night poyyuria and the high nitrogen excretion are characteristic.

Chronic Diffuse Nephritis

	Urine		Sodium Chlorid		Nitrogen	
Time of Day	c.c.	Sp. Gr.	Per cent.	Gm.	Per cent.	Gm.
8—10	230	1·022				
10—12	130	1·025				
12— 2	118	1·022				
2— 4	136	1·022				
4— 6	96	1·020				
6— 8	108	1·014				
Total Day	818			8·24		9·71
Night 8—8	950	1·014		7·61	0·73	7·14
Total 24 hours	1,768			15·85		16·85
Intake	1,760			8·50		13·40
Balance	−8			−7·35		−3·45

The results of a test meal during the stage of elimination of œdema. Note the large amount of fluid, salt, and nitrogen excreted.

CHRONIC DIFFUSE NEPHRITIS

Time of Day	Urine c.c.	Sp. Gr.	Sodium Chlorid Per cent.	Sodium Chlorid Gm.	Nitrogen Per cent.	Nitrogen Gm.
8—10	328	1·012				
10—12	174	1·011				
12— 2	248	1·014				
2— 4	279	1·101				
4— 6	88	1·013				
6— 8	100	1·011				
Total Day	1,217			4·08		9·88
Night 8—8	490	1·014		1·66	1·01	4·95
Total 24 hours	1,707			5·74		14·83
Intake	1,860			8·50		10·30
Balance	+153			+2·76		-4·53

The marked involvement of renal function is evident from the low fixed specific gravity.

THE SAME CASE ONE MONTH LATER

Time of Day	Urine c.c.	Sp. Gr.	Sodium Chlorid Per cent.	Sodium Chlorid Gm.	Nitrogen Per cent.	Nitrogen Gm.
8—10	216	1·009				
10—12	75	1·016				
12— 2	156	1·015				
2— 4	124	1·017				
4— 6	186	1·012				
6— 8	380	1·007				
Total Day	1,137			3·41		6·82
Night 8—8	400	1·007		1·52	1·17	4·68
Total 24 hours	1,537			4·92		11·50
Intake	1,760			6·20		13·40
Balance	+223			+1·27		+1·90

The marked clinical improvement is reflected in the result which closely approaches the normal.

To sum up then, involvement of the kidney function is first evidenced by changes in the night urine:

1. Increase in the amount—nocturnal polyuria.
2. Lowering of specific gravity.
3. Lowering in the percentage of nitrogen.

One or all of these phenomena may be present.

In severe cases marked functional impairment is indicated by:

1. Fixed and low specific gravity of day urine.

2. A diminished output of salt and nitrogen.
3. Tendency to a total polyuria.
4. Night urine of (a) Increased volume.
   (b) Low specific gravity.
   (c) Low nitrogen content.

In diffuse or parenchymatous nephritis the picture is a variable one—but gives much helpful information, as it does also in cardiac decompensation.

Were kidney entirely uninfluenced by extrarenal factors, the examination of the urine for urea and total nitrogen would be much more conclusive than it is, as an estimate of renal function. The data so derived gives general information of very positive value indeed, but is not to be interpreted as necessarily a quantitative estimate of renal damage.

Before leaving the subject of the urine one must refer to the test introduced by Rowntree and Geraghty[10] in 1910—phenolsulphonephthalein. It is an excellent test, easily carried out and simply read if one possesses even a very primitive form of colorimeter. Its use is based upon the knowledge that a definite amount of the dye is excreted in two hours in health, while with disturbance of function marked delay occurs in its elimination. In health 60 per cent. is eliminated in two hours. Suffice it to say that since its introduction it has received world-wide recognition and is to-day looked upon as an exceedingly valuable test, for both diagnosis and prognosis.

It is especially useful in surgical procedures on the kidney—where the comparative function of each kidney is of great importance.

Let us then turn to the other method of attack in studying renal disorder, and that is to see what degree of retention, if any, is present, in the blood, of those substances which the kidney normally excretes in adequate amount. At an earlier part of my remarks I referred to the end products of protein metabolism with which of course the kidney is very specially concerned, since one of its chief functions is the elimination of such waste products. They are grouped together under the name of non-protein, or incoagulable nitrogen, and in this term are included urea, ammonia, uric acid, creatinine, creatin, and an undetermined fraction which includes amino-acid nitrogen, and may be termed residual nitrogen.

The accompanying chart indicates their percentages of the total non-protein nitrogen in both blood and urine.

THE COMPARATIVE NITROGEN PARTITION OF URINE AND BLOOD IN PER CENT. OF TOTAL NON-PROTEIN NITROGEN AS INDICATED BY MYERS AND LOUGH[11]

Fluid.	Urea N.	Uric Acid N.	Creatinine N.	Creatin N.	Residual N.
Normal Urine	85	2	5	4	4
Normal Blood	50	3	2	0·3	46
Uræmic Blood	75	2·4	2·5	0·5	20
Nephritic	55	2·2	2	0·3	41
Gouty	50	6·0	2	0·3	42

These figures refer purely to the component parts going to make up the non-protein nitrogen and not at all to the amount of retention.

Progress along these lines of investigation is due largely to the work of Professor Folin[12] and his co-workers, also Frothingham,[13] Fitz,[14] Myers and Fine,[15] Benedict,[16] Foster,[17] Marshall,[18] and several other laboratory workers.

Normally these substances are found in the blood in a certain concentration, and if the kidney excretory power is markedly impaired it obviously follows that it will have difficulty in eliminating these very substances, upon the elimination of which it ordinarily expends so much of its energy, and that hence their concentration in the blood will increase.

Considering the most comprehensive first, non-protein nitrogen, Obermayer and Popper[19] first called attention to its increase in the blood in uræmic states. The normal amount in the blood is estimated as 25 to 30 mgms. per 100 c.c. although Gettler and Baker assign it an upper level of 45 mgms. In various kidney disabilities this may rise to over 350 mgms per 100 c.c. Frothingham and Smillie[13] have shown a very definite parallelism between the results of this and the phenolsulphonephthalein tests on the same cases.

Tileston and Comfort[20] in a very comprehensive study of one hundred and forty-two cases of considerable variety summarize as follows:

1. Fasting adults showed 22·9 to 25 mg. non-protein nitrogen per 100 c.c. of blood, and the urea nitrogen was 12 to 14 mg. per 100 c.c. of blood.

2. After full meals with meat there was a rise of 4·7 mg. of non-protein nitrogen and 2·5 mg. of urea nitrogen.

3. Cases of chronic nephritis, both interstitial and diffuse, without uræmia, showed moderate elevations, or were normal, while uræmic cases were all elevated.

4. Phenolphthalein tests were roughly proportional to the degree of retention, although some cases with good phthaleins showed retention.

5. Patients with over 100 mg. usually die within four or five weeks.

6. Nephritics with retention should have a restriction of protein which reduces the amount of retention.

7. In chronic passive congestion there is no retention of nitrogenous waste.

8. A marked elevation of N.P.N. makes a patient a poor operative risk.

9. Eclampsia seldom shows marked retention of N.P.N. and hence differs from true uræmia.

10. Compensated valvular disease, acute pericarditis, acute endocarditis, malignancy, typhoid, scarlet fever (uncomplicated), and acute rheumatism all gave normal values.

11. Thirty-six per cent. of all syphilitics examined, in various stages, showed a considerable degree of retention.

We may next turn to the urea of the blood, whose estimation has been rendered practical by Marshall with the urease prepared from the soy bean, which breaks up the urea and enables its estimation as ammonia. By reference to the table you will note the very large place which the urea occupies in the total non-protein nitrogen of the blood. Tileston and Comfort found it to be about 50 per cent. of the total N.P.N. in normal cases but in cases of marked retention the urea usually formed about 70 per cent. of it. They conclude that the determination of the total N.P.N. is of more value than the determination of the urea alone. Normal values for urea in the blood vary from 12 to 15 mgms. per 100 c.c.

The elimination of uric acid and its presence in the blood forms a very interesting chapter in pathological chemistry. In 1848, Sir A. B. Garrod[21] drew very interesting conclusions which are in surprising harmony with the views of to-day, especially when we consider the methods at his disposal. Until recently, no special advance has been made in the solution of this problem, and this advance is due to Folin's work and methods. Retention of uric acid even in large amounts, as evidences by recent methods of examination, does not necessarily lead to gout, but as Von Noorden[22] says, in addition to its retention there must be the accession of another unknown factor, before the deposition of uric acid occurs.

Uric acid is excreted by the kidney with greater difficulty than

is the case with other nitrogenous waste products, urea, and creatinine. Creatinine is excreted most easily, then urea and then uric acid. This fact is evidenced by the appended chart of Chace and Myers[23] which shows graphically the "staircase" effect produced by these phenomena. High uric acid content of the blood was frequently noted without retention of any other waste products.

Diagnosis	Condition	Mgms per 100 c.c. of blood			Phthalein 2 hrs. %	Syst. B.P.	Urine Alb.	Urine Casts
		Uric Acid	Urea N.	Creatinine N.				
Pulmonary tuberculosis. .	Unchanged	6·5	16	2·7	58	130	++	+
Pericarditis.....	"	5·6	13	2·1	45	150	-	-
Interstitial nephritis.....	"	5·5	12	2·5	37	185	-	+
Diffuse nepritis.....	"	9·6	19	2·4	45	175	+	+
Early interstitial nephritis..	"	9·5	25	2·5	13	185	+	+
Early interstitial nepritis....	"	6·6	24	3·3	26	185	-	+
Early interstitial nephirits..	"	8·7	20	3·6	20	100	+	+
Early interstitial nephritis..	"	6·3	31	2·0	23	150	-	-
Moderately severe chronic interstitial nephritis.....	Improved	8·0	80	4·8	0	240	++	++
		4·9	17	2·9	10	170		
Moderately severe chronic diffuse nephritis.....	Improved	8·3	72	3·2	25	238	+++	++
		5·3	21	1·9	43	145		
Moderately severe chronic diffuse nephritis.....	Improved	9·5	44	3·5	38	210	++	++
		2·5	19	1·9	52	120		
Typical fatal case of chronic interstitial nephritis.....	Died	22·4	236	16·7	0	210	++	pus
Typical fatal case of chronic interstitial nephritis.....	"	15·0	240	20·5	2—3	225	++	+
Typical fatal case of chronic interstitial nephritis	"	14·3	263	22·2	0	220	++	+
Typical fatal case of chronic interstitial nephritis.....	"	8·7	144	11·0	trace	225	+	+
Normal—uric acid		2—3 mg			per 100 c.c.			
urea		12—15 "						
creatinine		1—2.5"						

Since uric acid is eliminated with most difficulty, it follows, that its retention would likely be among the first evidences of disturbed function. The normal content of the blood is 2 to 3 mgms of uric acid per 100 c.c. of blood.

According to the above statements then, we would infer that

the retention of creatinine in the blood signified marked impairment of kidney function, since as Folin and Denis remark it is "removed by the human kidney with an ease and certainty, exceeded only by the facility of removal of the ammonium salts." Since it is so easily removed normally, its retention must mean very marked impairment of renal function. As already observed, creatinine on a meat free diet is entirely endogenous in origin and its formation is very constant. Hence a lowered nitrogen intake lowers the concentration of urea and uric acid, but does not influence that of creatinine. All cases, followed by Myers, with 5 mgms or over per 100 c.c. of blood have died. Normal values are 1 to 2·5 mgm. per 100 c.c. of blood.

URIC ACID IN THE BLOOD IN CASES OF INCIPIENT INTERSTITIAL NEPHRITIS.[23]

Diagnosis	Mg. to 100 c.c. blood			Phthalein 2 hrs.	B.P.		Urine	
	Uric Acid	Urea Nitrogen	Creatinine		Syst.	Diast.	Alb.	Casts
Interstitial nephritis.....	9·5	25	2·5	13	185	90	+	+
Fibrillation.....	9·3	14	2·9	44	120	90	-	-
Cirrhosis, nephritis, alcoholism..	8·7	20	3·6	20	100	87	+	+
General œdema	7·7	20	2·6	45	168	100	+	-
Carcinoma of stomach	7·5	16	2·2	50	150	90	-	-
Interstitial nephritis.....	7·1	16	2·0	26	185	110	-	+
Carcinoma of stomach	6·8	20	1·8	40	140	80	-	+
Pulmonary and kidney Tuberc .	6·5	16	2·7	58	130	90	++	+
Hypothyroidism and nephritis .	6·3	31	2·0	45	150	90	-	-
Syphilis and nephritis.....	6·3	17	2·7	38	185	80	++	+
Chronic arthritis and nephritis..	6·1	12	2·4	65	145	80	+	+
Pericarditis, alcoholism.....	5·6	13	2·1	45	150	65	-	-

Myers considers blood creatinine a much better prognostic guide than phthalein estimations, since the creatinine continues to show marked variations after the phthalein results are continuously negative, and hence variations in the patient's condition may still be taken cognizance of thus.

PROGNOSTIC VALUE OF CREATININE IN THE BLOOD OF NEPHRITIS.[23]

Cases	Blood Creatinine	Phthalein 2 hrs.	Termination
1	33·3	....	Died
2	28·6	0	"
3	22·2	0	"
4	20·5	2-3	"
5	20·0	0	"
6	20·0	0	"
7	18.9	0	"

PROGNOSTIC VALUE OF CREATININE IN THE BLOOD OF NEPHRITIS—*Continued*

Cases	Blood Creatinine	Phthalein 2 hrs.	Termination
8	17·8	....	Died
9	16·7	0	"
10	16·6	Trace	"
11	14·7	....	"
12	14·7	0	"
13	14·3	0	"
14	12·7	1	"
15	12·5	0	Stationary
16	11·1	3	Died
17	11·1	0	"
18	11·0	3 to 1	"
19	10·7	0–5–4–3–6	"
20	10·0	0	"
21	9·0	0	"
22	8·3	6–4–2	"
23	7·4	0	"
24	7·0	0	"
25	6·7	5	"
26	6·1	9	"
27	5·9	3	"
28	5·6	2–7–10	Improved
29	5·5	....	Died
30	5·4	13–4	Stationary
31	5·3	10	Died
32	5·2	....	"
33	4·9	....	"
34	4·8	0–10–31	Stationary

I should not conclude this part of my remarks without referring briefly to another method of estimation of the kidney function. I refer to Ambard's coefficient of urea excretion.[24] Ambard demonstrated that normally a constant relationship exists between the concentration of urea in the blood and the amount of urea excreted in a given portion of time, i.e., the rate of its execretion. In normal individuals this coefficient is held to be very constant but if the kidney function is impaired there is likely to be a relative increase in the concentration of urea in the blood and a relative decrease in its rate of excretion in the urine.

Ambard's first law is thus stated:

"If a constancy of the urea concentration in the urine is maintained, the square root of the urea eliminated in the urine in a definite interval is closely proportional to the concentrations of the urea in the blood." As variations in the concentration of urea in the urine alter the relationship of this to the urea concentration in the blood, Ambard formulated a second law to define the effect of this factor. His second law is: "If the blood urea remains at a constant concentration, the rate of urea excretion is inversely

proportional to the square root of the urea concentration in the urine."

The rate of elimination of urea also varies with the body weight, and is constant per kilogram of body weight, if other conditions are constant.

Ambard's formula is as follows:

$$K = \frac{U_R}{\sqrt{D\frac{20}{P}} \times \frac{\sqrt{C}}{\sqrt{25}}}$$

K —coefficient of urea excretion.
Ur —urea grams per litre excretion.
D —urea grams in urine in twenty-four hours.
C —urea grams per litre of urine.
P —body weight in kilograms.
70 —standard body weight in kilograms.
25 —standard concentration of urea grams per litre of urine.

The normal coefficient averages 0·080 and varies between 0·050 and 0·090. Deficiency in urea excretion results in higher values and this higher value is due to the changed ratio between urea concentration in the blood and the excretion by the kidney.

McLean[25] modified this formula by designating the ideal normal rate of excretion as 100 and his index in a given case then expresses "in direct percentage the rate of excretion found, in terms of the rate of excretion that a normal individual would develop under the same conditions as to the concentration in the blood, concentration in the urine, and body weight."

$$\text{Index of excretion} = \frac{D\sqrt{C} \times 8.96 \text{ (CONSTANT)}}{\text{Wt.} \times U_{R_2}}$$

D —grams urea excreted in twenty-four hours.
C —grams urea per litre of urine.
Ur —grams urea per litre of blood.
Wt —weight of body in kilograms.

The rate is not determined for twenty-four hours but for seventy-two minutes (i.e., $\frac{1}{20}$ of 24 hours).

The exact place these indices will assume in diagnosis and prognosis is by no means certain since very wide variations and discrepancies have been pointed out in individuals apparently in perfect health, by Addis and Watanabe.[26] Myers and Fine, as well as Jonas and Austin,[27] also criticize this method and claim the estimation of blood urea alone is more accurate, especially since slight carelessness in the collection of the urinary samples may very seriously affect the ultimate reading.

Mosenthal[28] has recently endeavoured to correlate some of the different tests of renal function and to indicate this approximately by + to + + + +, corresponding to slight, moderate, marked and maximal. I append his chart.

SCALE OF DEGREE OF IMPAIRMENT OF RENAL FUNCTION

Degree	Phthalein %	N.P.N. Blood mg. per 100 c.c.	Urea N. of Blood mg. per 100 c.c.	Ambard	Test Meal					
					Night urine		Variations in S. G. when highest S. G. is:			
					c.c.	s.g.	18	17 to 15	14 to 13	12
Normal	60+	30 –	15 –	0.090	400 –	18+	9+			
+ slight	59–40	31–45	16–27	0.0910 to 0.115	400–600	16 & 17	8 to 5	6		
++ moderate	39–25	46–65	28–44	0.116 to 0.220	600+	15 –	4 –	5 & 4	6+	
+++ marked	24–11	66–90	45–64	0.221 to 0.350	...	....	....	3 –	4 & 5	6+
++++ max..	10–0	91+	65+	0.351+	...	....	....	....	3 –	5 –

There is still another aspect of nephritis which is deserving of reference in view of recent methods of investigation. I refer to the subject of acidosis,[30] which quite apart from nephritis, has attracted so much attention of late, and especially in the cases of recurrent vomiting in children, which is looked upon as due to this condition. May I refer briefly to the underlying principles.

Normal metabolic processes require a circulating medium of very constant reaction. Normal blood reaction, like normal temperature, is one of the important physiological constants. This "reaction" of the blood is faintly alkaline, or its hydrogen-ion concentration is only slightly less than that of pure water. To L. J. Henderson[29] we owe our conception of this fact.

By hydrogen-ion concentration we mean that a solution is acid when it contains an excess of hydrogen over hydroxyl ions; neutral when hydrogen and hydroxyl ions are in equal numbers and alkaline when the hydroxyl ions predominate. In solution through the influence of the solvent (water) acids, bases, and salts, dissociate or ionize, and each ionized molecule becomes resolved into its positive and negative ions, and these are known as cations (+) and anions (—) carrying a positive and negative electrical charge respectively. The extent to which acids and bases ionize, since all do not ionize to the same extent, determines their strength as such. The application of this fact shall appear shortly.

Since cellular activity demands such a constant reaction, there must be some delicate regulatory mechanism which will rapidly respond to even very slight variations in the reaction and set in operation some process by means of which the normal reaction of the blood is restored. This sensitive mechanism is possessed by the respiratory centre. Pulmonary ventilation is increased over 100 per cent. by an increase in the hydrogen-ion concentration of the blood which is smaller than any known laboratory method may detect.

During metabolic activity there are added to the blood stream certain acid products, which are a volatile acid CO_2 excreted by the lungs and non-volatile acids, or "fixed acids" excreted normally by the kidneys. The normality of the blood reaction is maintained by the chemical composition of the blood and the excretion of these acid substances.

The chemical composition of the blood assists in this process owing to the large amount of weak acids and their salts which it contains, e.g. carbonic acid, phosphoric acid, sodium carbonate, sodium bicarbonate, monosodium phosphate, and disodium phosphate. Then in addition there are the proteins of both basic and acid properties. Indeed the balance of weak acids and salts is such as to allow the addition of the maximum amount of acid with the minimum change of reaction of the blood.

The above mentioned salts and alkali protein compounds constitute the alkali reserve of the plasma and any diminution of this alkaline reserve is known as acidosis, and is recognized by clinical symptoms, changes in the blood and alveolar air.

The chief acid product of normal metabolism is CO_2. A slight increase in its presence stimulates the respiratory centre causing added pulmonary ventilation and a return to normal with no depletion of the alkali reserve or "buffer" substances as Hender-

son named them. If, however, a non-volatile acid such as sulphuric, phosphoric, or betaoxybutyric acid is poured into the plasma some of this alkali reserve is used up and the reaction or hydrogen-ion concentration shifts toward acidity. This stimulates respiratory ventilation which being unable to remove non-volatile acids removes more CO_2 than normal to compensate for the increase in non-volatile acids which it is unable to remove, resulting in a lowered CO_2 content of the blood in the lungs, and hence of the alveolar air in contact with this blood, through the lung membrane. Then this blood with its diminished alkali reserve comes in contact with the tissues once more and receives the CO_2 normally produced, the change in the blood toward acidity is more marked and overstimulation of the respiratory centre again results. The body endeavours to replenish the alkali reserve by production of ammonia and by the selective excretion of acid by the kidneys, retaining the bases in the body to neutralize more acids. If, however, more acids continue to be poured into the plasma and the alkaline reserve is depleted in spite of all safeguards, the alkalinity becomes less and less and a point is reached which is incompatible with life and this point is practically neutrality.

Now as is evident from dyspnœa, many advanced cases of nephritis develop an acidosis, not so much due to the excessive formation of acids as in diabetes mellitus, but to the impairment of their normal elimination by the kidney. As an index of this condition the CO_2 tension of alveolar air was measured, since the CO_2 tension of alveolar air is the same as that of aerated blood leaving the lungs for the tissues. Another method was to test the hydrogen-ion concentration of the blood. However, recently Van Slyke[31] has introduced a fairly simple method of estimation of the CO_2 combining power of the plasma and several investigators have found this CO_2 combining power to be moderately to markedly reduced in diabetes and nephritis.

Now in closing I may say that the amount of blood required to do all of the tests for retention which I have indicated is not large—about forty cubic centimeters. It is easily secured and keeps very well on ice, and is not necessarily absolutely sterile.

My remarks have extended over more time than I had at first anticipated and there are some tests for the estimation of renal function to which I have not referred at all. Those I have not mentioned are not looked upon by our best trained investigators and clinicians as contributing much of value to our knowledge of this most fascinating subject of renal pathological chemistry.

Some of these tests may seem of too theoretical value to be of vital interest to the busy physician or surgeon, but one has merely to recall that the theoretical procedure of to-day is often the daily routine of to-morrow. A few years ago "acidosis" was a term seldom heard apart from diabetes and terminal nephritis, while now acetone bodies are commonly demonstrated in the urine of children quite apart from either of the above diseases.

But to the busy practising physician and surgeon may I commend the estimation, in all your patients with albuminuria, or high blood pressure, or œdema, of the two-hourly urine characteristics, while on some improvised series of test meals along the lines I have indicated. Accurately measure the quantity and specific gravity of both day and night urines, and watch for nocturnal polyuria with lowered specific gravity as an initial sign of impending trouble.

To this test add the phenolsulphonephthalein which is simply applied, and the colorimetric reading readily made on an apparatus available now for a few dollars. Adding this information to careful clinical observation you shall have obtained a very fair estimate indeed of the condition of that wonderful organ, the kidney.

I have purposely refrained from any attempt at classification of kidney disorders beyond the very rough one of interstitial and parenchymatous. An exceedingly interesting grouping of Volhard and Fahr promises to go far toward classifying more adequately than ever before the known clinical and pathological data of nephritis.

References:

1. Bayliss—"Principles of General Physiology." Longmans Green & Co., 1915.
2. Councilman, W. T.—"The Pathology of the Kidney." *Joural A. M. A.*, January 13th, 1906, p. 81.
3. Hawk, P. B.—"Practical Physiological Chemistry." P. Blakiston, 1916.
4. Myers and Fine.—"Essentials of Pathological Chemistry." *The Post Graduate.* New York, 1913, p. 36.
5. Mathews, A. P.—"Physiological Chemistry." Wm. Wood & Co., 1915, p. 717.
6. *Ibid.*—P. 717.
7. Barton, W. M.—"Manual of Vital Function Testing Methods and their Interpretation." Badger, 1916, p. 75.
8. Hedinger and Schlayer.—*Deutsch. Arch. F. klin. Med.*, 1914, cviv, 120.
9. Mosenthal, H. O.—"Renal function as measured by the elimination of fluids, salt and nitrogen, and the specific gravity of the urine." *Arch. Int. Med.*, xvi., 1915, 733.
10. Rowantree and Geraghty—*Jr. Pharm. and Exper. Therap.*, i, 1910, 579.
11. Myers and Lough—"The Creatinine of the blood in nephritis and its diagnostic value." *Arch. Int. Med.*, xvi, 1915, 545.
12. Folin and Denis—*Jr. Biol. Chem.*, 1913, xiii, 469; xiv, 29; 1914, xvii, 487.

13. Frothingham and Smillie—"The relation between the phenolsulphonenphthalein excretion in the urine and the non-protein nitrogen content of the blood in human cases." *Arch. Int. Med.*, 1914, xiv, 541. "A Study of different nitrogenous diets in chronic nephritis." *Arch. Int. Med.*, 1915, xv, 204.

14. Fitz—"The Value of Tests for renal function in early and advanced Bright's Disease." *Amer. Jr. Med. Sc.*, 1914, cxlviii, 330.

15. Myers and Fine—*Jr. Biol. Chem.*, 1913, 1914, 1915. "The Significance of Uric Acid, Urea, and Creatinine of the Blood in Nephritis." *Arch. Int. Med.*, 1916, xvii, 570.

16. Benedict, S. R.—*Jr. Biol. Chem.*, 1915, xx, 629. "Uric acid in its relations to metabolism," 1916, ii., 1, *Jr. Lab. and Clin. Med.*

17. Foster, N.B.—*Arch. Int. Med.*, 1912, x, 414. "Functional Tests of the Kidney in Uræmia," *Arch. Int. Med.*, 1913, xii, 452.

18. Marshall, E. K.—*Jr. Biol. Chem.*, 1913, xiv, 283. *Ibid*—287.

19. Obermayer and Popper—*Zeit. F. klin. med.*, 1909, lxvii, 332.

20. Tileston and Comfort—"The total non-protein nitrogen and the urea of the blood in health and disease as estimated by Folin's methods," *Arch. Int. Med.*, 1914, xiv, 620.

21. Garrod, A. B.—"Observations in certain pathological conditions of the blood and urine in gout, rheumatism and Bright's disease." *Med.-Chirurgical Transactions*, 1848, xxxi, 83.

22. Von Noorden C.—*Metabolism and Practical Medicine*, 1907, iii, 669.

23. Chase and Myers—*Jr. A. M. A.*, September 23rd, 1916, lxvii, 929.

24. Ambard, L.—*Comp. rend. Soc., de Biol.* November 19th, 1910, p. 411, 506.

25. McLean, F. C.—*Jr. Ex. Med.*, 1915, xxii, 212, 366.

26. Addis and Watanabe, *Jr. Biol. Chem.*, 1916, xxiv, 203.

27. Jonas and Austin—"The value of the Ambard quotient in the estimation of renal function," *Amer. Jr. Med. Sc.*, 1916, clii, 560.

28. Mosenthal, H. O.—*Jr. A. M. A.*, September 23rd, 1916, lxvii, 933.

29. Henderson, L. J.—*Ergebn d. physiol.*, 1909, viii, 254.

30. Acidosis, Different Aspects of."—

(a) Woolley, P .G.—"Acidosis," *Jr. Lab. and Clin. Med.*, i, 1916, 712. "Acidosis in Nephritis," *Ibid.* xx, 620.

(b) Peabody, F. W.—"The Acidosis of Chronic Nephritis," *Arch. Int. Med.*, 1915, xvi, 955.

(c) Levy and Rowntree—"A Study of the buffer value of the blood," *Arch. Int. Med.*, 1916, xvii., 525.

(d) Scott, R. W.—"The dissociation curve as an index to the hydrogen-ion concentration of the blood." *Jr. Lab. and Clin. Med.*, vol. i, 1916, 608.

(e) McLeod, J. J. R.—"Clinical methods for determining the buffer action of the blood," *Jr. Lab. and Clin. Med.*, 1916, ii, 54.

31. Van Slyke, Stillman and Cullen—"*Proc. Soc. Exper. Biol. and Med.*, 1915, xii, 165.

FRACTURES OF THE SKULL FROM A NEUROLOGICAL STANDPOINT

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IT is necessary to confess at the outset that there are no neurological phenomena pathognomonic of fracture of the skull. The nervous symptoms that accompany fracture of the skull are not in essence due to that fracture, but result from injury to the intracranial contents and may be brought about by other lesions than a broken skull—any severe blow on the head, for example.

Such a blow on the cranium produces what we call concussion. It temporarily squeezes or crushes the brain. An animal's brain may be seen to be squeezed out into a trephine opening made for purposes of observation, if a blow is struck on the opposite side of its skull. Owing largely to the fact that the brain rests on a water cushion formed by the cerebro-spinal fluid, this compressing force affects the whole brain and not merely the site of the blow. The resulting rise of intracranial pressure tends to squeeze out the fluid contents of the skull and interferes for the time with the intracranial circulation. This interference with the cerebral circulation, combined with the effects produced upon the cells comprising the various nerve centres, is probably responsible for the initial symptoms of concussion, symptoms which vary greatly in intensity.

In the mildest cases there are transient giddiness, headache, flashes of light and ringing in the ears. In cases of moderate severity there are added to the above symptoms flaccidity of all the muscles and rapid unconsciousness, shallow breathing and weak pulse, followed perhaps by brief incoherence as consciousness returns, also complaint of headache, giddiness and tinnitus, an unsteady gait and a sense of fatigue.

In the more severe cases of concussion, to which a majority of the cases of fracture of the skull belong, there is sudden and profound unconsciousness, with great pallor, muscular relaxation and loss of reflexes, even, it may be, that of the pupils to light. Probably in the earliest stages the patient is pulseless and does not breathe, while wounds do not bleed. This very brief preliminary

stage is rarely to be seen by a skilled observer. The pulse returns, weak and irregular at first, and shallow, irregular breathing is established. The blood pressure is low.

Many of the fatal cases of fracture of the skull never rally from the shock of this first stage.

Our experience at the Western Hospital is that the struggle in what prove to be the fatal cases of fracture of the skull is apt to be a short one, for of sixty fatal cases in the hospital records forty-five (or 75 per cent.) died on the day of the accident or the day following.

But in most of these fatal cases as well as in cases that recover, the bulbar centres (vasomotor, cardiac, and respiratory), stimulated by their anæmic condition, are urged to greater effort. Through vagus stimulation the heart becomes slower and stronger, respiration becomes deeper and stertorous, though often irregular or of Cheyne-Stokes type, and through action of the vasomotor centre upon vasomotor nerves the blood vessels contract. All this results in a rise of blood pressure considerably above normal.

The deep reflexes return and are frequently quite active. The patient begins to move and moans a little. Consciousness returns gradually. The patient is apt to be irrational for a time and is very irritable, often noisy, and strongly resents being examined or disturbed in any way.

Careful examination of the nervous system is necessary, in order that no localizing symptom may be overlooked—prolonged and profound mental disturbance in lesions of the frontal lobe, motor paralysis or Jacksonian attacks in Rolandic lesions, hemianopia in occipital lobe lesions, paralysis of the various cranial nerves. Sensory symptoms do not seem to be common and are hard to make out, owing to the patient's mental condition, but I have noticed some astereognosis in one or two cases.

But it is important to remember that such localizing lesions may be due to a focal inflammatory œdema, as well as to hæmorrhage or to bony pressure. I well remember the case of a young man who, after receiving a very severe blow on the left side of the head, followed by headache, loss of power to do his usual mental work and a marked rise of blood pressure, developed a decided weakness of his right arm. I was tempted to advise operation, but the negative finding on lumbar puncture led to a policy of watchful waiting which the event justified, for the weakness soon disappeared spontaneously.

Perhaps the commonest focal sign of value is the presence of

a Babinski. The existence of dorsal flexion of the great toe on tickling the sole of the foot should be regarded with suspicion, even if present but for a short time.

It is remarkable how trifling may be the injury which will occasionally fracture a skull. For example, an Italian was taking down from a scaffold a board which he could readily reach from the ground. The end of the board, slipping, fell a distance of not more than eighteen inches, striking him on the head and knocking him down. He was brought to the Western Hospital and was quite conscious on admission, but soon became drowsy. When I saw him a couple of hours after admission, he had a one-sided Babinski and could hardly be roused. The lumbar puncture showed blood in the cerebro-spinal fluid. Immediate preparation was made for operation, but before this could be done, he stopped breathing. Fortunately a few artificial respirations and a large hypodermic of strychnine and atropine started him breathing again, and the operation was completed by Dr. Springle. The skull in the temporal region, which was of almost egg-shell thinness, was fractured. A large quantity of clot and semi-fluid blood was removed, partly intradural, but mainly of middle meningeal origin. Two days later the man was sitting up in bed calling for his dinner and he recovered completely.

Lumbar puncture in cases of suspected intracranial traumatism should always be resorted to. The presence (and the amount) of blood in the cerebro-spinal fluid and the increased tension the fluid is generally under are important guides to treatment. It is of some advantage to know the percentage of blood contained in the fluid withdrawn, and where the time necessary to do a cell count is lacking, a quicker approximate estimate may be made by measuring the hæmoglobin in the cerebro-spinal fluid and comparing this with the percentage of hæmoglobin in the patient's blood.

As to *Prognosis*, recovery is gradual and tedious. In most cases giddiness, more or less vasomotor instability, headache and inability to do as much physical or mental work as before the accident, are symptoms that last for months.

Our experience at the Western Hospital would seem to show that the danger to life is soon over in the majority of cases. Only ten of our sixty fatal cases lived more than three days, and but three lived more than five days after the accident. It is to be remembered in this connexion, however, that in a large proportion of our cases the violence of the blow was very great (tramway or railway accidents).

Dr. England tells me that in a general way it is his experience that, provided a case of fractured skull does not die as a direct result of the injury, those cases do best where the bone is severely crushed and the membranes and even the brain substance are badly lacerated—possibly because such cases are sure of good drainage. He refers to the cases of an old man and his wife, both struck by a street car some years ago. The man had only a dislocated clavicle and a lacerated hand. He died. His wife arrived at the Western Hospital with her head smashed in, very pale, with sighing breathing, apparently moribund. Pieces of bone were removed from as deep as the ventricles. The confident prediction was made that she could not live through the night, but she was conscious next day and made an uninterrupted recovery, complete except for a hemiplegia due to destruction of the motor area.

Dr. Springle has a similar case showing to what an extraordinary extent the brain may be damaged and recovery occur. A tramway trolley was pulled from its wire, so that the pole flew into the air, throwing off the end, weighing some twelve pounds. This fell on the head of a boy of nineteen, crushing in the vault of the skull. He was brought to the Western Hospital "in a dying condition", to quote the note made on his admission, brain, scalp and skull being intermixed in a horrid mess. Forceps had to be left for days in his brain as deep as the lateral ventricle, to control hæmorrhage. He recovered and two or three years later when examined for medico-legal purposes he had no paralysis whatever.

Bigelow's case of a man of twenty-five who had a crow-bar three feet seven inches long and one and one-quarter inches in diameter blown completely through his head, entering below the left zygoma and passing out near the coronal suture close to the middle line, reported in 1850, is still a most remarkable case, for the man was able to sit up and converse almost immediately after the accident and recovered completely except for blindness of his left eye.

Our Western Hospital statistics seem to show that women, though much less liable to fracture of the skull than are men, are a little more apt to die from it. Among one hundred and forty-five cases, twenty-four were females, of whom eleven died, twelve recovered, and one left the hospital on the day of admission (mortality 48 per cent.): of one hundred and twenty-one males, forty-seven (or 39 per cent.) died.

The complications to be feared are mainly infective, such as meningitis, abscess and sinus thrombosis, and need not detain us. A certain amount of inflammatory œdema of the brain and its

membranes occurs in practically all cases and is an occasional cause of death.

So much for the prospect as to mortality. What is the outlook as to completeness of recovery?

In almost all cases certain symptoms of the so-called neurasthenic type last for some time—headache, impairment of memory, vasomotor instability, irritability, a sense of mental and physical exhaustion, and disinclination for exertion. In most cases I think such manifestations are due to real brain injury. These symptoms usually subside in time, though convalescence may take many months.

There are also various permanent disabilities which may be grouped together as due to destruction of brain tissue—aphasia or paraphasia, anosmia, hemiplegia and other paralyses, hemianopia or amblyopia. Mental symptoms occur in cases where the frontal region is affected and range from partial loss of memory to violent insanity or feeble-mindedness.

Finally, there is that considerable group of unfortunate cases where traumatic epilepsy follows the injury. The fits may not appear for some time after the accident.

Brief illustrations of some of these nervous sequelæ of fracture of the skull may be cited from the Western Hospital records.

Persistent neurasthenic symptoms with severe headache, giddiness, depression, and incapacity for mental or physical work lasted two or three years with very little improvement in a bricklayer who fell from a height on his head.

A boy aged fifteen following fractured skull had hemianopia and frequent epileptic fits with some mental deterioration. He had refused operation.

A girl aged seventeen struck by a locomotive had a depressed fracture of the frontal bone. The bone was raised, but the dura was not opened. Normal mentally before the accident, after it she was positively silly, refusing to let anyone "look at her pretty eyes," etc. Her memory too was almost nil. She was unable to find her way about the city alone and several months after the accident failed to remember (after an interval of two weeks) ever having seen the physician in regular attendance upon her.

Doctor Springle's case, already referred to, where extreme laceration of the brain occurred, showed a tendency to loss of self-control, undue suspiciousness and mental deterioration. This young man also took epileptic fits, first beginning some time after

the accident, and had a prolonged series of fits (status epilepticus) which almost ended fatally.

Under the head of prognosis some reference should perhaps be made to the subject of blood pressure. It must be admitted that the information given by the study of blood pressure in fractures of the skull must be interpreted in correlation with other symptoms. But this much may be said: *sudden* changes in blood pressure are to be regarded with suspicion and a sudden or comparatively rapid drop particularly is most ominous and frequently precedes a rapidly fatal termination. Let me quote one illustrative case here.

A very heavily built man, aged fifty-six, fell upon his head a considerable distance to the floor of an ice-house and fractured the base of his skull. Admitted to the Western Hospital at 10.30 he had a blood pressure of 178, which by 10.55 had fallen to 154. The cerebro-spinal fluid contained blood, his breathing was getting more laboured and he was becoming rather cyanosed, but he insisted on delaying somewhat the immediate operation that was strongly advised, until other members of his family could arrive. At 11.20 B.P. was 143; at 11.48 (when operation was begun) B.P. 120; at 11.53 B.P. 115; at 12.00 B.P. 108; at 12.03 B.P. 99; 12.10 B.P. 93; 12.13 B.P. 88; 12.16 B.P. 80; 12.19 B.P. 75. Right up to this time pulse and respirations were practically unchanged, about 120 and 24 respectively. At 12.19 B.P. was 75, pulse became uncountable, and respirations ceased suddenly. Three minutes later, under artificial respiration, B.P. was 60. Artificial respiration was kept up nearly three quarters of an hour to no effect.

The *Treatment* of fractures of the skull is essentially a surgical question, and any suggestions I make along these lines are made with proper diffidence; but my colleagues, Dr. England and Dr. Springle, to whom I wish to express my sincere thanks for permitting me to use the large amount of valuable material from their clinics for the purposes of this paper, have given me such excellent opportunity to follow up all these cases to a termination that even one who is not a surgeon may say this much.

Though every case of fracture of the skull does not require operation, every such case requires the closest observation, for developments that will necessitate immediate operation may take place very rapidly. If operation is decided on, it is of no use whatever to explore the wound without opening the skull, and unless the hæmorrhage is entirely extradural (which seems rather rare), it is of very little use to open the skull without opening the dura.

And, if you wish to decompress, take away enough bone to accomplish your object. A trephine opening an inch across will not afford much room for a compressed brain to expand and the brain is much more apt to be damaged by laceration when the opening is small than when it is of ample size. The patient will not die for the lack of two or three square inches of skull, but he may by keeping too much of his skull lose his life.

Cases are well known in which a fractured limb, to which plaster was immediately applied directly to the skin, later swelled up, became gangrenous and required amputation. Is it not possible that, in cases where considerable inflammatory swelling of the brain and its membranes follows the contusion and laceration caused by the injury, non-interference or half interference may result in somewhat the same effect on the cerebral circulation as the plaster had on the circulation in the rapidly swelling leg, the skull splinting the swollen brain as the plaster did the leg? And remember that any considerable increase of the intracranial over the intraspinal pressure is apt to crush the medulla into the foramen magnum like a tight-fitting cork into a bottle. Also, the medulla, containing as it does all the important vital centres, stands such pressure very badly. I well remember an autopsy on one case of fracture of the skull where this jamming of the medulla into the foramen was present to such an extent that the groove made by the ring of bone pressing on the medulla was distinctly visible.

Apart from the danger to life, I have an impression—it is hardly an opinion for which I could quote you convincing reasons—that on the whole, cæteris paribus, cases operated on recover more completely and more rapidly than unoperated cases, and are less likely to have permanent ill-effects, such as epilepsy.

Certainly some cases that for a time apparently do not require operation lapse into such a condition that they must be operated on or die; and occasionally cases occur which one could wish had been operated on, though they were not.

In this connexion, emphasis may be laid upon the frequency with which cases of injury to the cranium supposed to be of a trifling nature have been admitted to the Western Hospital, cases the symptoms of which have become gradually more severe and which would undoubtedly have caused death if operation had not been resorted to in time to save the patient.

One such case that occurred two or three months ago may be briefly quoted. Kept over night in the Out-door department after

a fall, this middle-aged woman was taken to the ward because she hardly seemed well enough to send home. Rather dull and stupid, she was thought to be somewhat lacking mentally, and little attention was paid to her. Her dulness increased, however, and when Dr. England's attention was drawn to her two or three days after her admission, upon his return after an absence from town, she was unable even to tell her own name. When I saw her immediately after, she was not unconscious, though she had incontinence of urine and fæces and nothing that was said to her seemed to reach her understanding. She had, I think, a low blood pressure, and blood-stained cerebro-spinal fluid came away under pressure on lumbar puncture. Operation by Dr. England removed a considerable quantity of dark semi-fluid blood from inside the dura and she made a perfect recovery.

Apart from operative measures, the treatment of fractures of the skull from a neurological standpoint is essentially that of concussion. In this respect it is only necessary to emphasize the importance of complete rest and liquid diet for a sufficiently long time.

THE second convocation of the American College of Physicians will take place at the Hotel Nassau, Long Beach, Long Island, on June 5th, 1917. About ninety per cent. of all the Fellows who have not entered on duties connected with the war are expected to be present. About fifty physicians of national repute will be admitted to Fellowship.

THE honour of being the first woman from the overseas Dominions, and the seventh woman in Great Britain, to pass the first part of the examination for the London degree of F.R.C.S. and L.R.C.P., has fallen to Miss Marian Noel Bostock, daughter of Senator Hewitt Bostock, Liberal leader in the Senate. Miss Bostock at present is acting house physician in the Queen's Hospital for Children at Hackney, London.

Editorial

FINCH AND BAINES—A SEVENTEENTH CENTURY FRIENDSHIP*

IT is with great pleasure that we call the attention of the readers of this JOURNAL to a book which has just been issued by the Cambridge University Press. The author is Archibald Malloch, a Graduate in Medicine of McGill in 1913, at present a temporary Captain in the Canadian Army Medical Corps. Letters from Captain Malloch have already appeared in this JOURNAL, both from Dunkirk where he served as Surgeon with the Friends' Ambulance Unit; and afterwards from La Panne where he worked under Dr. Depage. The name Captain Malloch bears is well known in Canada. He represents in his family a second generation of Medicine: and it is to his father, Dr. E. M. Malloch of Hamilton, a pupil and disciple of Lister, that his book is dedicated.

As Captain Malloch himself puts it, "a chance of this War placed me in the summer of 1915 in charge of a small Hospital for Officers at Burley-on-the-Hill in Rutland—" England's smallest county. This was for many years the seat of the Earls of Winchilsea and Nottingham, whose family name was Finch; and here it was that opportunity came to Captain Malloch to collect the material for his record of the past. He tells us of the life-long friendship of Thomas Baines and John Finch, and in telling us of this he tells us also of many other things. Finch and Baines were a kind of David and Jonathan. Neither of them was married; and each gave the other the sort of friendship, the sort of whole-hearted

*FINCH AND BAINES: A SEVENTEENTH CENTURY FRIENDSHIP. By ARCHIBALD MALLOCH, B.A., M.D., temporary Captain, Canadian Army Medical Corps. Publishers: C. F. Clay, Cambridge University Press. London: Fetter Lane, E. C. Toronto: J. M. Dent & Sons, Ltd. 1917. Price 10|6.

affection, that in our hurried, hustling age seems almost to have disappeared from the earth. In this history there is, as always, other history. In telling us of the friendship Captain Malloch takes us along with him backward to where Science, emerging from its swaddling-clothes, shows itself as an energetic infant, manifests itself as a living growing thing. We are back in the time of the Stuarts, of Oliver Cromwell, of the Restoration.

There is some doubt as to the date of the birth of Sir Thomas Baines, the elder of the two friends; but if, as is currently reported, he was born in 1622, then he was born in the same year as Molière, arch-delineator of the Physician and the Scientist—pompous and be-wigged—of his day. Amongst much these same Physicians and Scientists lived Finch and Baines; but as we read Captain Malloch we become aware that to Molière's picture, as to every other picture, there is another side. Sir John Finch and Sir Thomas Baines were be-wigged certainly, but they were neither ignorant nor pompous. They were emphatically human beings, not so very unlike ourselves, eagerly seeking answers to those same questions which are on every side of us to-day—too many even yet unsolved: and as we read we are drawn to these two seventeenth-century men, full to the brim as they were with the modern scientific spirit—the desire to know.

Happily for us Sir John Finch kept a diary. Not the emotional kind of diary kept by eighteenth-century heroes and heroines, but a very concise and practical record of his doings and thinkings. From this and from his letters to his sister—Anne Conway, reputed the most learned of the "female metaphysical writers" of the time, and called by her brother always "dearest Soule" or "dearest Dear"—we can trace, by Captain Malloch's good offices, the every-day life of a man divided from us by three long centuries; and that in the intimate fashion which is the only way worth tracing anything. Captain Malloch indeed, in bringing together these records, enables us to test the truth of Balzac's remark

that, when history is written as it ought to be, there will be no need of fiction. Balzac perhaps had in mind the kind of history which Captain Malloch gives us here.

Sir John Finch and Sir Thomas Baines met at Christ's College, Cambridge, and there as students together they formed their life-long friendship. After leaving the University they went abroad together: visited at Paris the "Hostel Dieu" and found it "a famous Hospital but there's eight in a bed"—which gives some ground for Molière's animadversions on the Profession!—and from thence they made their way, by Auxerre, Dijon, Geneva, to Padua. There they worked, studied, and wrote and from there in 1652 Finch began to send to his sister and brother-in-law "Discourses" on philosophical and scientific subjects: a custom he kept up for the rest of his life. He seems to have interested himself in every conceivable thing. He writes of the "Manner by which Trees, Plants and all Vegetables are Nourished"; he writes of the circulation of the blood and ranges himself on the side of Harvey—a connexion by the way of his own—although he persists in retaining relics of the pre-Harveian idea that the blood ebbed and flowed in both the arteries and veins; he discusses the way to make "a choice Coffé for your friends" and the Philosophy of Descartes, and he sends his sister "three of Descartes *Principles*" together with two "Bolognia masty dogges"; he also transcribes a Latin poem by Baines in praise of Molinetti, Professor of Anatomy at Padua. Poems have been written on all kinds of things but "Anatomical dissections publicly performed by Antonio Molinetti of Padua" seems a queer choice for verse! Such a choice, however, did Baines make, and a long Latin poem did he write. "You do not, Molinetti, dissect bodies," he says in the course of it, "but adorn them. You bring them into the Theatre cleansed from all dirt, perfect in limb, and the obedient muscles are freed at your touch; thus you show yourself not an anatomist, but, what is far greater, a god." Walt Whitman himself could not have said more.

The friends lived lives full of recognition. Academic Honours were theirs almost for the asking. Finch in 1660 or thereabouts came under the notice of the Duke of Tuscany and was appointed Professor of Anatomy at Pisa—the first and only Englishman to receive this honour. Later he was appointed Physician to the Queen of England, later still Ambassador to Florence. The friends were knighted one after the other, each received the Degree of Doctor of Physic from Cambridge, and they both interested themselves in the formation of the Royal Society, "a society for promoting experimental philosophy": in 1764 Sir John Finch was sent as Ambassador to the Ottoman Court. All his life Finch knew what it was to have money, power, social recognition: he was emphatically what is called a successful man. His friend accompanied him everywhere, and as life went on these two men seem to have become more and more wrapped up in one another, more and more careless as to the rest of the world. Finch undoubtedly was the David of the alliance, the active energetic partner. "In public," says Captain Malloch, "Finch always appeared as the leader of the two, but to what extent he was indebted to his helpmate Baines, for his success in diplomatic and scientific work, we shall never know." As to Sir Thomas Baines, we hear of him principally as engaging himself in diligent reading and note-taking. He filled the post of Professor of Music at Gresham College for many years, mostly *in absentia*. and though, as his biographer says, "there is no evidence to show that he was qualified to hold any musical professorship at all," hold it and its emoluments he did just as he wrote his Latin poem on dissection. These men lived in a blessed age where Specialism was not!

The book is full of entertaining anecdote. On one occasion while Sir John Finch was Ambassador in Constantinople, the French Ambassador, warmed by wine and like a giant refreshed, was moved, we are told, to relate at lunch some of the incidents of his early life in Paris. Baines, a gentle soul,

was much discomposed by these revelations, and, leaning forward, he interrupted them by asking, "Et che dirà il Crucifisso?" Finch, who always took great pride in any observation of his friend, states that the Frenchman was "struck dumbfounded and was filled with astonishment." It cannot but strike *us* that the rest of the lunch must have been somewhat of a strain for all concerned.

In 1681, Sir Thomas Baines died at Constantinople, and Sir John Finch was left alone. "I have lost Sir Thomas Baines," Finch writes, "the best friend the world ever had." David did not long survive Jonathan. Sir John Finch returned home with the body of his friend, and died in the following year at London.

The book is admirably printed on paper that, in these lean days of War, it is a pleasure to touch and handle, and it is full of illustrations, reproductions of portraits of the friends, and of places connected with their lives. Sir John Finch, in his portrait by Carlo Dolci, has all the appearance of the successful man: and evidently he knew what it was to look arrogant. Sir Thomas Baines has by far the more charming face. He has meditative eyes, a gentle expression; and in spite of his habit of asking difficult questions, most surely he was lovable. "I shall live, O beloved," says Sir John Finch in the epitaph he wrote on his friend, "mindful of our Friendship, and no day shall ever remove us from a remembering age."

So ends the story of the friendship between Sir John Finch and Sir Thomas Baines. Captain Malloch tells us that this "pleasant but quite novel task" was undertaken at the suggestion of Sir William Osler. "I owe a great debt of gratitude for his influence,which has been a continual stimulus," says Captain Malloch, and in the concluding sentence of the Preface, he designates Sir William Osler "the young man's friend."

Ability to accomplish work such as the biography of these two friends is given to few of us: to still fewer is given

the wish to attempt such a piece of work in the midst of a busy life. Captain Malloch has had the wish, and it is evident that he has enjoyed the work, for his book bears the marks of pleasure in the writing of it—the only real reason for ever writing anything at all. Such an author earns the admiration and gratitude of his readers. This JOURNAL offers Captain Malloch its sincere congratulations.

THE ACTIVITIES OF A PROVINCIAL ASSOCIATION

THE presidential address of the Manitoba Medical Association by Dr. James McKenty, of Winnipeg, put forward a strong plea for support of the Canadian Medical Association and its JOURNAL by the various provinces. The Manitoba Association became affiliated with the Canadian Medical Association in 1912, and since that time the annual fee of $5.00 includes membership in the two Associations and the subscription to the CANADIAN MEDICAL ASSOCIATION JOURNAL. Fifty cents out of every annual fee of five dollars is refunded to the affiliated Provincial Association of the province from which it came. This refund constitutes the only revenue of the Manitoba Association. This year it amounted to $58.00. At present, therefore, there are only 116 out of the 519 resident practitioners in Manitoba who are subscribers to the JOURNAL and members in good standing of the two Associations. It was pointed out that this showing was not creditable to the province, and that a National Association was necessary for the promotion of many of the aims of the profession, and a journal essential to the maintenance of a vigorous association. Such aims as the control of quackery, the patent medicine fraud, and the enactment of legislation relating to public health matters can best be furthered by such an organization. In respect to these matters a great work had been accomplished in the United States by the American Medical Association and its journal. In Canada a similar work was needed, and, in addition, there

were already problems arising out of the world war which must be met. The organization for doing this existed in the Canadian Medical Association and its JOURNAL. In order to assist in this work a more loyal support must be extended to the National Asspciation. The JOURNAL was the mouthpiece of the profession in Canada, and on its own merits was worthy of support. He who would keep himself informed regarding the attitude of the profession towards public questions needs the JOURNAL.

A review of Manitoba's contribution to the present great world struggle yielded a creditable showing. Since the beginning of the War the province had contributed for military service 226 graduates in medicine and 113 trained nurses; of these about fifteen of the medical men were on the permanent staff doing duty in the province.

Another matter for consideration was the policy to be adopted towards the claims certain irregular practitioners are now making for legal recognition by the province. The speaker was convinced that a policy of uncompromising opposition would be a mistake. In the first place we could never hope to free the province completely from quackery. The conditions which favour its growth cannot be removed. At best some lessening of the susceptibility of the community could be brought about by a diffusion of knowledge upon matters of health. Something was being done by the Manitoba Board of Health in this direction. Through the agency of specially trained nurses in the employ of the Board, who visit the people in their own homes, "instruction was being given, and practical demonstrations wherever possible, upon all matters relating to the health and care of children, domestic sanitation, and community health." This was a work which ought to receive the cordial support of the profession in Manitoba. Secondly, under democratic government such as was in force there, the jury which finally decides such matters is the general public, and such a jury was known to be utterly incompetent to judge of the merits of such a question.

The spirit of democracy also was opposed to laws limiting the freedom of the individual. The evidence establishing the need for such a law must be amply adequate and readily appreciated by the public in order to secure its enforcement after it has been enacted. Without the support of public opinion it becomes more or less a dead letter. A policy therefore should be adopted that would appeal to the common sense of the average man. It was felt this could be done without impairing the efficiency of the regulation proposed. The people of Manitoba had already sanctioned laws based upon the principle that he who claims to be an expert in repairing the defects of a machine must have an accurate knowledge of its construction and the functions of its various parts. An Act should be framed applying the same principle to the individual claiming to be an expert in repairing the ailments of the human machine so that after he has satisfied the University of Manitoba as to the accuracy of his knowledge in anatomy, chemistry, physiology, pathology, bacteriology and diagnosis he should be permitted to practise the healing art under whatever name he chooses. And while amendments were being made to the Act its prohibitive features should be made more stringent and more comprehensive. This policy would disarm those who have visions of trades unionism and, if adopted, it would protect the community from imposture, in so far as this could be done by legislation. Such a policy has long since rendered homœopathy harmless, and might be relied upon to do the same for osteopathy and all other forms of therapeutic aberration.

It was pointed out that in the Province of Manitoba the authority to issue license to practise, to investigate charges and cancel licenses for cause, and to prosecute illegal practitioners, was vested in the College of Physicians and Surgeons of Manitoba. All of these were surely matters of much interest to the practitioners of the province, yet at the last election for membership in the Council of the College (September, 1916), only eighty out of approximately five hundred

votes were cast. This indicated that something was wrong either with the profession or with the College. Was the difficulty a lack of interest on the part of the profession in the matters the College is authorized to deal with? Or was there a lack of confidence in its ability to deal with them successfully? Is the difficulty the annual fee of two dollars which the members must pay in order to vote? Should this fee be made compulsory for a continuation of the license or should it be abolished altogether? It was suggested that each member of the Manitoba Association give this subject some thought and come to the next meeting of the Association prepared to propose some means for increasing the efficiency of the business organization of the profession in Manitoba.

A FEDERAL DEPARTMENT OF PUBLIC HEALTH

WTH commendable persistence and with the courage born of conviction, Dr. Michael Steele, the member for South Perth, on May 2nd, again introduced in the House of Commons the question of the establishment of a Federal Department of Public Health. The importance of the matter has been pointed out over and over again in this JOURNAL, and the lessons we have learnt during the war have made us realize even more acutely than before the failure of our present system of guarding the public health. We live in a new country, in a country that has been developed, and in cities that have grown up, since a knowledge of the laws of hygiene and health were acquired; and yet, out of 407,221 men, of an age when they should be at the height of their physical power, 43,453 were found physically unfit for active service! The war has impressed upon us another lesson which is of particular interest to the medical profession and the Government, and that is the value of health, both from the national and the economic standpoint, and the importance of preserving the life of future citizens who will some day take the place of those who have laid down their lives in the ser-

vice of their country. In spite of all that has been done hitherto to prevent the spread of such diseases as tuberculosis, how many people die from preventable disease during the course of one year; and how many infants die whose lives might be saved? The success that has attended the measures already taken, and particularly those in force among the troops taking part in the present war, gives us the answer. Again, the war is teaching us a third great lesson, and that is the vast importance of utilizing our resources. The food shortage in Europe is already acute and on this continent the situation is becoming more and more urgent,—and in Canada only about one-tenth of the land area is under cultivation. Our resources, naturally, cannot be developed unless our population is increased and for this we must rely to a large extent upon immigration; it must be, however, the immigration of healthy and efficient individuals and not, as has happened so often in the past, of the inefficient and the feebleminded.

Though at the moment all our energies are centred upon the prosecution of the war and it may be impossible to effect comprehensive and lasting changes until our main object is accomplished, let us look forward to the time when these different matters, all of which exercise so vital an effect upon the public health, shall be coördinated under one efficient department.

Among the many honours that have fallen to the lot of Colonel H. S. Birkett, C.B., M.D., none perhaps will be more appreciated by his friends than the compliment recently paid him by the placing of his name upon the Editorial Committee of the *Journal of Laryngology, Rhinology and Otology*. Not only is it a tribute to the professional standing and ability of Colonel Birkett, but a compliment to the medical profession of Canada in that Colonel Birkett is the first Canadian to receive this distinction.

ACCORDING to the returns tabled in the House of Commons by Sir Edward Kemp, the Minister of Militia, on May 7th, men to the number of 407,221 were enlisted in the Canadian Expeditionary Force up to March 31st, 1917, and out of that number 43,453 were rejected as being medically unfit for active service. The rejections include men who have been incapacitated by wounds and the figures are made up in the following way: men discharged in Canada, exclusive of those who have returned from abroad, 29,658; men who have returned to Canada and have been discharged as medically unfit, 11,917; and those who have been discharged overseas, to the number of 1,478. Thus the percentage of rejections throughout Canada was 24. The figures for the various military districts in the provinces of Ontario and Quebec are given as follows: Military district No. 1 (London), 15,886 men accepted out of 20,544, or 77 per cent.; military district No. 2 (Toronto) 58,086 accepted out of 73,664, or 76 per cent.; military district No. 3 (Kingston-Ottawa), 19,792 accepted out of 28,046, or 68 per cent.; military district No. 4 (Montreal), 11,261 accepted out of 18,050, or 63 per cent.; military district No. 5 (Quebec), 3,292 accepted out of 4,246, or 77 per cent.

Miscellany

Books Received

THE following books have been received and the courtesy of the publishers in sending them is duly acknowledged. Reviews will be made from time to time of books selected from those which have been received.

CLINICAL AND LABORATORY TECHNIC. By H. L. MCNEIL, A.B., M.D., adjunct professor of medicine and instructor in physical diagnosis, University of Texas Medical School, Galveston. With illustrations. Publishers: C. V. Mosby Company, St. Louis, 1916. Price, $1.00.

THE NEWER METHODS OF BLOOD AND URINE CHEMISTRY. By R. B. H. GRADWOHL, M.D., director of the Pasteur Institute of St. Louis; and A. J. BLAIVAS, assistant in the same. 226 pages with sixty-five illustrations and four colour plates. Publishers: C. V. Mosby Company, St. Louis, 1917. Price, $2.50.

PREVENTIVE MEDICINE AND HYGIENE. By MILTON J. ROSENAU, professor of preventive medicine and hygiene, Harvard. With chapters upon SEWAGE AND GARBAGE, by G. C. WHIPPLE; VITAL STATISTICS, by JOHN W. TASK; MENTAL HYGIENE, by T. W. SALMON. Second edition thoroughly revised, 1209 pages. Publishers; D. Appleton & Company, New York and London, 1916. Price, $6.00.

THE DISEASES OF INFANCY AND CHILDHOOD. For the use of Students and Practitioners of Medicine. By L. EMMETT HOLT, M.D., Sc.D., LL.D., professor of diseases of children in the College of Physicians and Surgeons (Columbia University), New York; and JOHN HOWLAND, A.M., M.D., professor of pediatrics in the Johns Hopkins University, Baltimore. Seventh edition, fully revised. 1161 pages with 215 illustrations. Publishers: D. Appleton & Company, New York and London, 1916. Price, $6.00.

Obituary

JOHN L. DAVISON, M.D.

THE following appreciation of the late Dr. Davison has been received from Dr. H. B. Anderson, of Toronto:

Dr. John L. Davison, of Toronto, died at the residence of his brother, W. S. Davidson, Esq., in Napanee, on April 20th, 1917, where he had gone to spend the Easter holidays. Dr. Davison had been in indifferent health for some years being a victim of angina pectoris. The immediate cause of his death was pneumonia.

Born in 1853, Dr. Davison was the youngest son of John and Jane (Swanzy) Davison, who came to Canada about 1815 from Co. Antrim, Ireland, and settled at Odessa, Frontenac County. As a boy he attended the public school at Yarker; afterwards he studied at the Newburgh Grammar School and the Toronto Normal School, where he was awarded the McCabe Gold Medal. He was a teacher in the Provincial Model School, Toronto, for ten years, during which time he graduated in Arts in 1880 in the University of Toronto. He then studied Medicine in Trinity Medical College, where he graduated in 1884, afterwards pursuing post-graduate studies in Edinburgh and London, where he took the M.R.C.S. qualification. Returning to Canada he began practice in Toronto in 1885. The same year he was appointed Professor of Pathology in the Women's Medical College, and the following year Professor of Materia Medica and Therapeutics in Trinity Medical College. Appointed visiting physician to the Toronto General Hospital in 1887, he relinquished this post in 1907 in order to facilitate what was considered would be a satisfactory reorganization of the staff of the hospital, and was appointed to the consulting staff. On the federation of Trinity with the University of Toronto in 1902 he became Professor of Clinical Medicine in the latter institution. For many years he was editor of the *Canada Lancet*. On the organization of the Imperial Life Assurance Company he was appointed medical referee; later also he became consulting referee to the Manufacturers Life.

Dr. Davison was a member of the Masonic Order and of the National, Toronto, York and Tadanec clubs. In politics he was a Conservative; in religion a Presbyterian; he never married.

In the death of Dr. Davison the medical profession of Canada has lost one of its most esteemed and distinguished members. After beginning practice in Toronto, he soon became established as one of the best known and highly regarded physicians of the city, and his popularity, not alone with his patients, but with his medical confrères and the public at large, continued to increase until the time of his death. The reasons for his success are not difficult to appreciate. His handsome appearance, distinguished and dignified bearing, his direct, straightforward and honourable attitude toward all with whom he came in contact, his kindly and philosophic outlook on life, were all features of a unique personality which attracted and retained warm friendships. Highly endowed by nature, he had the further advantage of a thorough general and professional education, extended by travel and intercourse with people prominent in social, educational, political, and business affairs.

He was an excellent clinical teacher and lecturer, the breadth and soundness of whose judgement made a deep impression on his students. He was the ideal type of the cultured and skilful family physician, eminently fitted to be "friend, counsellor, and guide" to his large and influential clientèle. It must be rare indeed that one is rewarded with a deeper hold upon the confidence and affection of those to whom he ministers, or who seek advice in their troubles. His friends were legion, and included all ranks and classes of society, —men and women, old and young, rich and poor—all came under the spell of his broad human sympathy, kindliness of heart and sparkling humour. For ten years he lived under the shadow of angina pectoris, which confined his activities within a steadily narrowing sphere, yet, without complaint, he adjusted himself to enforced limitations, which, however, never abated the joy of living. In fact, his last years he repeatedly said were the happiest of his life, his physical disability giving him more leisure for reading, reflection and for music, especially of the violin, at which he passed many pleasant hours with a small set of intimate friends.

He was an expert with rod and gun, and it was exhilarating to watch the boyish enthusiasm with which he prepared for his frequent outings to the Georgian Bay, where he revelled in the beauties of nature in the company of kindred spirits at the Tadenac Club. On hearing of his death, Dr. George T. Elliot of New York, one of his companions of the Tadenac, wrote as follows:

"It was a great shock; it was a terrible sorrow and a deep realization of irreparable loss I experienced and felt when the fact

was brought in to me that our dear old friend, the sweetest-natured friend and companion ever, had been called away and had left us behind—yes, to follow him eventually—but still without his company. Alone has he gone from those he loved and who loved him, and it is with deep sadness I am writing you my feelings, knowing how you also were close and dear to him. What a pity he has gone, and how we will miss him—not for a day or a month—but for all the time that still remains to us, his cheeriness, his loveableness, his kindly smile and overbrimming milk of human kindness will be a cherished memory. May God bless him."

In accordance with his wishes and in keeping with his simple tastes, he was buried in the family plot in the pretty cemetery on the banks of the Sydenham River, near the village of Florence, where his boyhood days were spent, and whence a number of his old friends accompanied the remains to pay their last tribute of love and respect.

LIEUTENANT-COLONEL HEWETSON, M.D.

Lieutenant-Colonel Samuel W. Hewetson, C.A.M.C., whose death occurred on March 6th, at the Royal Free Hospital, London, after an operation, had been on active service for about a year. In August, 1914, he was in practice at Pincher Creek in Alberta, and upon the declaration of war, immediately offered his services to his country. He was appointed regimental medical officer of a battalion that was going overseas, and later A.D.M.S. of Military District No. 13. He was anxious, however, to get to the front and when the Eighth Field Ambulance was authorized, he was given command of that unit and in due course proceeded overseas. The strain of his military duties told upon him severely and some time ago it was reported that he was suffering from nervous breakdown and shell shock, and later came the report of his death. Lieutenant-Colonel Hewetson was in the forty-ninth year of his age and was unmarried. He had practised for a time at Calgary before going to Pincher Creek, and was a graduate of McGill University of the year 1893.

MAJOR DAVID B. BENTLEY, M.D.

Major Bentley, whose death occurred in England early in April, volunteered his services as soon as war had been declared and was appointed to the command of the Fourteenth Field Ambulance.

Some months were spent in training at Valcartier and when the first contingent of the Canadian Expeditionary Force left for England, Major Bentley with his unit accompanied it. After a year's hard service at the front he returned to England and for a time was on duty at Monk's Horton. Later he was appointed to take charge of the medical base hospital depot at Southampton. His health, however, had been seriously undermined while at the front and he never regained his strength. A few months ago he entered the Granville Special Canadian Hospital at Ramsgate and it was there that his death occurred. David Bentley was born in 1864, and took his degree at Trinity Medical College in 1891. He was in practice at Sarnia, Ontario, and was well known as a physician throughout the western part of the province, where he was also district medical officer of health. He leaves a widow and two sons, both of whom are on active service.

Dr. Thomas Sparks, of St. Mary's, Ontario, died on April 10th, after a long illness. He was a graduate of the University of Toronto, where he took his medical degree in 1867, and practised for some years at Lakeside, in the province of Ontario. From Lakeside he went to St. Mary's about twenty-five years ago and continued to practise until about five years ago. His son, Captain G. Lindsay Sparks, C.A.M.C., of London, Ontario, is on active service.

Dr. Henry James Fixott, who died on April 11th, was in the seventy-third year of his age and had been in practice at Arichat, Nova Scotia, for almost fifty years. Dr. Fixott came of an old Jersey Island family, his father and grandfather before him being of the medical profession and the latter serving at one time as surgeon in the British Army. He graduated from the Harvard Medical School in 1866.

Dr. Wallace G. King, of Buctouche, New Brunswick, died suddenly on April 21st. He had been in poor health for some time, but seemed to be improving and had resumed work, and it was upon his return from visiting a patient that he suddenly expired. Dr. King had been in practice at Woodstock for thirty-two years and will be greatly missed by his patients, to whom he had endeared himself by his unselfishness and devotion to duty. He was sixty-seven years of age and is survived by a widow, three sons and three daughters.

DR. JAMES A. ROSS, of Barrie, Ontario, died on May 1st, in the fifty-second year of his age. He was born in Oro Township the son of the late James Ross, at one time Warden of the County, and received his medical degree from the University of Toronto. He completed his medical studies at Edinburgh and Glasgow and upon his return to Canada took up practice as an eye, ear, nose and throat specialist. He had practised at Barrie since 1895, but for the past twelve months had been in poor health. He never married. His brother, Captain W. A. Ross, C.A.M.C., is at present in France and another brother, Captain Victor Ross, C.A.M.C., was sanitary officer at Niagara Camp last year.

DR. JOHN BUCHANAN WILSON, who died at Ottumwa, Iowa, on April 20th, was a Canadian by birth and a graduate of the University of Toronto.

DR. H. E. HAMMILL, of Assiniboia, died suddenly at Weyburn on Saturday, April 14th. Dr. Hammill was the son of Mr. J. D. Hammill, mayor and postmaster at Meaford, Ontario. He was in practice at Assiniboia and was about thirty-two years of age. He leaves a widow.

DR. NEIL ROY STEWART, who also died suddenly at Weyburn on April 14th, was in practice at East End, Saskatchewan, until a short time ago when he was appointed medical officer of the 249th Battalion. He subsequently severed his connexion with the battalion, however. Dr. Stewart was born in 1889 and graduated from the University of Manitoba in 1914.

DR. E. L. GRAVES died at Mount Bridges, Ontario, on March 5th, of pulmonary tuberculosis. Dr. Graves received his degree from Western University Medical School in 1914.

News

ONTARIO

DR. M. F. E. GRAHAM, who has been assistant physician in charge of the women's wards at the Eastern Hospital for the Insane at Brockville for the past two years, has been appointed

resident physician of the Jubilee Hospital at Victoria, British Columbia.

THE members of the Separate School Board, Toronto, at a recent meeting, unanimously decided to ask Dr. Hasting to undertake the medical inspection of children attending schools under the jurisdiction of the Board. In future therefore, pupils in attendance at school in Toronto—whether Protestant or Catholic—will be subject to medical examination under the direction of the Board of Health.

DR. E. C. AXFORD, formerly of Ripley, has gone into practice at Alvinston.

QUEBEC

THE annual meeting of the Alexandra Hospital, Montreal, took place on April 20th, when the report for 1916 was submitted by the president, Sir Thomas Roddick. During the year 973 patients were treated in the hospital, including 347 cases of diphtheria, 317 cases of measles, 48 cases of erysipelas, and 38 cases of poliomyelitis; 53 deaths occurred, 35 of them taking place within forty-eight hours of admission.

ALBERTA

THE plans for an addition to the Ponoka Asylum are in course of preparation.

IT is the intention shortly to open a hospital at Fort McMurray.

THE Holy Cross Hospital at Calgary is to be enlarged.

SASKATCHEWAN

IT was decided at a meeting of the Saskatchewan Hospital Board, which took place on May 2nd, that alterations and improvements should be made to the General Hospital and that an isolation hospital should be erected to replace the shacks now in use for cases of infectious disease.

MEDICAL COLLEGES

Toronto University

A SPECIAL convocation was held at the University of Toronto on May 2nd, on which occasion degrees in medicine were conferred upon students to the number of thirty-two, many of whom had already been on active service and had returned to complete their course in medicine. The recipients of the degree of M.B. were: York Blayney, B.A.; James S. Crawford; Nicholson W. Furey, Henry R. Hargrave, James H. Howell, B.A.; Harold J. Irvine, Cecil O. Miller, Wm. T. B. Mitchell; A. E. Mackenzie; John W. Mackenzie, Charles Russell MacTavish, H. C. Nash, Harry A. Rawlings, J. Whittier Reddick, C. V. Scott, B.A., Percy R. Shannon, Frank R. Smith, Geo. F. Skyes, Elfred C. Tate and Charles A. Wells. Degrees were conferred in absentia on: Ruth C. Cale, B.A.; Mary E. D. Johnston, E. G. Berry, A. J. Butler, C. K. Fuller, B.A.; J. A. R. Glancy, W. Hall, B.A.; Robert Morley Harvie, George D. Jeffs, B.A.; J. L. King, F. W. Leech, and B. S. Loney.

McGill University

THE annual convocation took place at McGill University on May 11th, when the degrees of M.D., C.M., were conferred upon the following gentlemen, sixteen in number. G. W. Bissett, Vancouver Island, British Columbia; A. N. Chisholm, Port Hastings, Cape Breton; H. A. DesBrisay, Shaughnessy Heights, Vancouver; A. C. Farlinger, B.A., Ft. Covington, New York; H. L. Gokey, South Hammond, New York; J. P. Hadfield, Fall River, Massachusetts; R. S. Hall, Jamaica; J. F. Haszard, Charlottetown; W. A. Hunter, Huntingdon, Quebec; A. F. McGregor, New Glasgow, Nova Scotia; A. P. Murtagh, Ottawa; W. S. Parsons, Montreal; E. E. Rogers, Vancouver; B. W. Skinner, Weston, Nova Scotia; L. J. Stuart, Brantford, Ontario; C. G. Sutherland, New Glasgow, Nova Scotia.

The candidates have already seen active service but returned to Canada to complete their studies. It is now their intention as qualified practitioners to offer themselves to the C.A.M.C. for further service at the front.

The prizes awarded for the session 1916-17 were:

THE HOLMES GOLD MEDAL, for highest aggregate in all subjects forming the Medical Curriculum: H. A. DesBrisay, Vancouver.

*Final Prize for highest aggregate in the Fifth Year Subjects: O .V. Marsh, Jamaica, B.W.I.

*Wood Gold Medal for best examination in all the Clinical branches: T. M. Richardson, B.A., Balderson, Ontario.

*These candidates received their degrees in February, 1917.

Dalhousie University

The annual convocation at Dalhousie University was held on May 10th, in the Library Hall, Studley, Halifax.

The following seven candidates received the degrees of M.D., C.M.: Thomas Roland Dwyer, Holyrood, Newfoundland; Roy Dickson Lindsay, Halifax; Joseph Percy Macgrath, Tusket, Nova Scotia; Philip Doane McLaren, Halifax; Thadeus Sieniewicz, Fairview, Nova Scotia; Solomon Jacob Turel, Halifax; Andrew Fraser Weir, New Glasgow, Nova Scotia.

It is probable that several of the graduates will join the C.A.M.C.

ARMY MEDICAL SERVICES

Among the Canadians recently decorated by the French War Office for distinguished and conspicuous services in France were the following members of the Canadian Army Medical Corps:

Croix de Chevalier. Lieutenant-Colonel Arthur Mignault, of Montreal.

Croix de Guerre. Captain Arthur Chester Armstrong, of Alexander, Manitoba.

The following appointments in the Canadian Army Medical Corps were gazetted on April 28th, last.

Lieutenant-Colonels to be temporary Colonels: Kenneth Cameron, D. O. McPherson, F. G. Finley, W. L. Watt, R. D. Rudolf, C. F. Wylde, L. M. Simpson.

Lieutenant-Colonels to be temporary Colonels: F. Etherington as officer commanding Canadian General Hospital in France; J. D. Courtenay as officer commanding Canadian Special Eye and Ear Hospital; E. C. Hart as officer commanding General Hospital; W. W. Nasmyth.

Majors to be temporary Lieutenant-Colonels: E. R. Brown, R. Raikes, H. C. S. Elliott, A. J. Mackenzie, D. A. Clark, C. E. Doherty, R. A. Bowie, F. Guest, E. S. Ryerson.

Majors to be temporary Lieutenant-Colonels while so employed: D. P. Kappelle as officer commanding Canadian Cavalry Field Ambulance; J. A. Amyot, consultant in sanitation; T. A. Starkey, sanitation officer; R. Wilson, consultant *x*-ray medical electricity; L. E. W. Irving, officer commanding Canadian Convalescent Hospital.

Captains to be temporary Majors: J. T. Hill, W. H. Tytler, W. Bethune, J. D. Morgan, R. H. Sutherland, G. H. R. Gibson, H. E. MacDermot, S. Ellis, G. W. O. Dowsley, J. C. Calhoun, F. A. C. Scrimger, R. H. McGibbon, C. R. Graham, A. K. Haywood, W. A. G. Bauld, J. G. W. Johnson, F. H. Mackay, C. H. Robson, D. E. Robertson.

Other promotions are: To be Lieutenant-Colonel: Major J. J. Fraser, of Walkerton, Ontario, officer commanding No. 2. Field Ambulance, C.E.F.

Captain G. Russell Reid, C.A.M.C., Toronto, has been appointed medical officer of the 253rd Battalion.

Colonel J. A. Roberts, C.A.M.C., who has been in command of the Duchess of Connaught Canadian Red Cross at Cliveden, has been appointed to the command of the Canadian Hospital at Basingstoke.

Colonel W. L. Watt, C.A.M.C., of Winnipeg, is now in command of the Cliveden Hospital and Lieutenant-Colonel J. McCombe, C.A.M.C., has been appointed A.D.M.S. Canadians at London.

Lieutenant-Colonel H. E. Munroe, C.A.M.C., has been appointed to the command of the Canadian Military Hospital at Hastings. Colonel Munro, as will be remembered, has been in command of No. 8 Stationary Hospital, which was mobilized under his direction.

Lieutenant-Colonel E. S. Ryerson, C.A.M.C., has been appointed A.D.M.S., of the Toronto Military District in succession to Colonel Marlow.

Major S. A. Smith, D.S.O., has resigned his commission in the C.A.M.C. in order to accept an appointment in the R.A.M.C.

THE Royal Red Cross of the first class has been awarded by His Majesty the King to Miss Elizabeth Russell, matron of the Duchess of Connaught Canadian Red Cross Hospital at Cliveden. Miss Russell is a daughter of Dr. James Russell, of Hamilton.

THE Royal Red Cross of the second class has been awarded by His Majesty to Nursing Sister Helena MacLaughlin and Nursing Sister Isobella D. Strathy.

MAJOR D. A. CLARK, C.A.M.C., of Toronto, who has been attached to Canadian medical headquarters at London, is now A.D.M.S. Canadians, at Bramshott. Colonel Bridges, C.A.M.C., has left Bramshott and is now A.D.M.S. at Shorncliffe, in succession to Colonel Rennie who is returning to Canada.

THE following physicians recently completed a course in military training at Vancouver and a number of them have volunteered for service with the Canadian Army Medical Corps: Drs. T. A. Wilson, D. J. Bell, J. H. Carson, Corry R. McKenzie, N. Allen, W. E. Newcombe, Bagnall, D. A. Thompsett, O. S. Large, W. A. McTavish, J. J. Mason, S. Harvey, J. W. Ford, Ernest P. Fewster, W. B. Burnett, J. Gillespie, W. L. Coulthard, E. Bolton, J. Mair Robertson.

CASUALTIES

Died on Service

LIEUTENANT - COLONEL SAMUEL WILLIAM HEWETSON, C.A.M.C.

CAPTAIN ADAM PEDEN CHALMERS, C.A.M.C., of Toronto, died May 26th, in Bermuda.

Wounded

COLONEL J. J. FRASER, C.A.M.C., of Walkerton, Ontario.

MAJOR G. J. BOYCE, C.A.M.C.

CAPTAIN R. J. GARDINER, C.A.M.C.

CAPTAIN G. R. JOHNSON, C.A.M.C.

CAPTAIN A. H. WALLACE, C.A.M.C., of Chilliwack, British Columbia.

LIEUTENANT R. S. STONE, C.A.M.C., of Chatham, Ontario.

Canadian Literature

Original Contributions

The Canada Lancet, March, 1917:

The importance of renal functional tests in surgery	C. H. Hair.
Enucleation of the eyeball	E. A. Hall.

Le Bulletin Médical de Québec, March, 1917:

Deuxième promenade mélancholique à travers les cimetières de Québec	E. Nadeau.

L'Union Médicale du Canada, March, 1917:

Observations cliniques. Complications cardio-arterielles au cours de la fièvre typhoide—pneumonie et pression arterielle	J. E. Dubé.
Contusion du rein	B. G. Bourgeois.
Cours de therapeutique appliquée à la Faculté dé Médecine Laval, Montréal. Le régime alimentaire dans les maladies organiques	D. Masson.
Etiologie de la fièvre typhoide. Les porteurs de germes	C. E. Dubuc.

The Western Medical News, January, 1917:

Syphilis and general practice	V. E. Black.
Oblique inguinal hernia in infants	W. A. Robertson.

The Public Health Journal, March, 1917:

The value of milk depots	J. Tessier.
Meningococcus meningitis	J. G. Fitzgerald.
Modern conceptions of fumigation after communicable diseases	F. Adams.
The economic value of preventive medicine	J. O. McCarthy.

Medical Societies

NEW BRUNSWICK COUNCIL OF PHYSICIANS AND SURGEONS

THE annual meeting of the Council of Physicians and Surgeons of New Brunswick was held in Fredericton on April 19th, 1917. Those present were: T. F. Sprague, M.D., Woodstock; J. D. Lawson, M.D., St. Stephen; S. C. Murray, M.D., Albert; Thomas Walker, M.D., St. John; W. W. White, M.D., St. John; A. F. Emery, M.D., St. John; L. M. Curren, M.D., St. John; G. C. Van Wart, M.D., Fredericton; John S. Bentley, M.D. (the Registrar), St. John.

The following officers were elected for the ensuing year: president, L. M. Curren, M.D., St. John; treasurer, A. F. Emery, M.D., St. John; registrar, John S. Bentley, M.D., St. John.

The professional examiners and various committees were appointed. The professional examinations will be held in St. John twice each year commencing on the fourth Wednesday in June and on the fourth Wednesday in January. Much business of a routine nature was transacted. The next meeting of the council will be held at St. John in July, when the New Brunswick Medical Society will be in session.

TORONTO ACADEMY OF MEDICINE

AT the annual meeting of the Academy of Medicine, which was held in the Academy Building, 13 Queen's Park, Toronto, on May 10th, the following officers and members of Council were elected for the session of 1917-18: President, Dr. D. J. Gibb Wishart; vice-president, Dr. A. Primrose; honorary secretary, Dr. J. H. Elliott; honorary treasurer, Dr. J. H. McConnell; past president, Dr. John Ferguson. Chairmen of sections—Medicine, Dr. G. W. Ross; Surgery, Dr. W. A. Cerswell; Pathology, Dr. F. W. Rolph; State Medicine, Dr. Gordon Bates; Ophthalmology and Oto-Laryngology, Dr. F. C. Trebilcock; Pediatrics, Dr. George E. Smith; Drs. A. H. Perfect, H. B. Anderson, F. N. G. Starr, J. G. Fitzgerald, Wm. Goldie, C. P. Lusk, W. A. Young and B. P. Watson.

PETERBOROUGH MEDICAL SOCIETY

A MEETING of the Peterborough Medical Society was held on March 22nd, with a large number of members present, not only the city but the surrounding towns being well represented. On this occasion the paper of the evening, on Pyelitis, was given by Dr. Fraser, of Montreal. After the discussion which followed, Drs. Cameron and Gallivan, on moving a hearty vote of thanks, paid a warm tribute to Dr. Fraser on the excellent manner in which he had treated his subject and said it was with great pleasure that the Society had welcomed one from their own county, who was making a name for himself in the medical world.

THE MONTREAL MEDICO-CHIRURGICAL SOCIETY

THE eighth regular meeting of the Society was held in the Montreal General Hospital on Friday, January 19th, 1917. The meeting took the form of a clinical evening, the members of the Society being the guests of the Medical Board of the Hospital. After the programme refreshments were served; there were ninety-eight members present.

PROGRAMME

PART I.—CLINICAL CASES

(Surgical Amphitheatre)

1. "Recurring intestinal obstruction," Dr. Hill.
2. (a) "Vaquez's disease;" (b) "Tumour of the liver," Dr. Lafleur.
3. "Charts from cases of transfusion," Dr. Henry.
4. "The galvano-cautery in the treatment of larnygeal tuberculosis," Dr. Craig.
5. "Tumour of the mouth," Dr. Hamilton.
6. (a) "Coxa vara and valga;" (b) End results of operations upon the carpal bones," Dr. Nutter.
7. "Selected skiagrams," Dr. Wilkins.
8. (a) "Sarcoma of the kidney;" (b) "Tuberculosis of the ilio-cæcal region," (c) Regeneration of shaft of femur," Dr. Barlow.
9. (a) "Traumatic epilepsy;" (b) "Imperforate anus;" (c) Bone graft of humerus;" (d) "Pressure upon trachea by enlarged thyroid. Child of eight years," Dr. Pennoyer.
10. (a) "Graves' disease without enlargement of the thyroid gland;" (b) "Concealed tuberculosis;" Dr. Gordon.

11. (a) "Actinomycosis." (b) "Results of polor ligation and partial excision of thyroid in Graves' disease," Dr. von Eberts.

12. (a) "Vesical calculus in a child three and a half years old;" (b) "Pyonephrosis vesical fistula," Dr. Powell.

13. "Differential diagnosis between tic and chorea," Dr. Shirres.

14. (a) "Evulsion of tubercle of tibia;" (b) "Gunshot injury of humerus," Dr. Smythe.

PART II.—DEMONSTRATIONS

1. *X*-ray department." Dr. Wilkins.

2. "Series of eye cases. No. V. operating room." Dr. Mathewson.

3. "Pathological specimens. Governors' Hall." Dr. Scott.

THE ninth regular meeting of the Society was held Friday, February 2nd, 1917, Dr. W. S. Morrow, president in the chair.

PATHOLOGICAL SPECIMENS: Series by Dr. Horst Oertel.

These specimens are from an interesting and unusual case of lymphatic leukæmia in the service of Dr. Martin. The patient was a girl of eight years, admitted to the hospital on November 15th and died January 29th, so that the course of the disease was a short one. She had sought admission for cough, pain in the stomach and enlarged glands and the disease is said to have commenced six weeks before admission and five days after tonsillitis. Then the right parotid gland began to swell, followed by swelling of the left and of the submaxillary glands. One week later a cough developed and sputum appeared after a few days; she had chills and night sweats but had not lost weight or colour. Femoral glands also became enlarged.

Physical examination on admission to the Royal Victoria Hospital showed general glandular enlargement, but no increase in size of spleen. Blood pressure, 115 systolic and 80 diastolic. Liver palpable. Urine pale, amber, acid, sp. gr. 1020. The blood examination was interesting from the start: after admission, on November 16th, the red blood cells were 2,400,000, whites 27,400 and hæmoglobin 54 per cent. The red blood cells decreased quite rapidly so that at the end of January, shortly before death, they had dropped to 690,000; hæmoglobin to 18 per cent., a severe anæmia; while throughout there was a corresponding increase in lymphocytes, from 27,400 to 201,000. The increase in lymphocytes was almost entirely on the part of typical, small lymphocytes,

so that here we have a rather exceptional picture of acute lymphatic leukæmia in which the increase in white blood cells is due to small typical lymphocytes, as contrasted with the usual acute lymphatic leukæmia, in which the prevailing leucocytes are of the large lymphoblastic or myeloblastic types. The polymorphonuclears at the beginning were only 12 per cent., the small lymphocytes, 57½ per cent.; later the polymorphonuclears dropped to 4 per cent., while the small lymphocytes rose to 82 per cent., transitional 2 per cent., undetermined 8 per cent., myelocytes about 2 per cent. So that we can, perhaps, speak in this case, following Leube's terminology, of a leukanæmia.

Autopsy disclosed several additional interesting facts. In the first place there existed a general, very marked, lymphoid hyperplasia in conformity with the usual anatomical findings of the lymphatic leukæmias. The lymph glands are markedly enlarged but are discrete and remain individual; the gross character of the lymph glands varies; the peribronchial glands are very pulpous, splenic, while the enlarged lymph glands of the mesentery and other parts are white, firm, and pale. Similar to those of the peribronchial variety are those in the mediastinal region.

The spleen on the other hand is small and shows very limited lymphoid hyperplasia which impresses one more as infiltrative in character. It seems that here the spleen has not taken an essential part in the formation of lymphoid cells. The thymus is well preserved, large, extremely firm, solid and well outlined, and microscopically shows its tissue almost entirely replaced by what appears to be lymphoid infiltration, so much so that it is difficult to find any thymus structure at all.

The bone marrow was distinctly reddish at autopsy and showed, microscopically, overgrowth of well-differentiated lymphoid cells, mostly small; very few myelocytes, great loss of red blood cells, but hardly any new red blood formation.

The last point of interest is the condition of the kidney. It is well known that in all leukæmias there is leucoblastic infiltration into the kidney. In this case it is so to a most extraordinary degree. This kidney weighs over 400 grams, which would be, even for an adult, a kidney of considerable size and weight. It is uniformly enlarged, bulging, perfectly smooth, pale white, with distinct hæmorrhagic areas and streaks, mottled. Microscopic sections show very diffuse and extensive infiltration by lymphocytes so great that in certain parts medulla and cortex have been almost entirely obliterated and the kidney substance looks entirely like lymphoid tissue.

For some time a discussion has been going on whether the lymphoid nodules and infiltration which occur in leukæmias are really true infiltrations or local lymphoblastic or myeloblastic foci. I think in these it is safe to assume that the largest number of cells are directly derived from the blood; one can see them early, perivascular in origin, and from these places they infiltrate into the tissue spaces and into the surrounding substance, primarily between the tubules, and ultimately replace them. The liver shows much smaller foci.

Discussion: Dr. F. M. Fry: I saw the leukæmic case in my office some weeks before admission (sent to me by Dr. Viner) and advised that she be brought to hospital for further study. The child presented then a most striking enlargement of the salivary glands and she was anæmic and seemed to have all the symptoms described by Mikulicz years ago. It is known that these cases show a pseudo-leukæmia which later progresses to a true leukæmia that proves fatal, as in this child.

Dr. C. F. Martin: One very interesting feature about this case was that five days before the onset of symptoms there had been a tonsillectomy which naturally associates the disease with the idea of an infection. In the early stage of the disease there was not much lymphocytosis. We made a temporary diagnosis of general enlargement of the parotid glands and cervicals of infectious origin. The fact that the condition was of long standing excluded more or less the diagnosis of mumps. We then discussed Mikulicz's disease but the absence of any condition around the lacrymal glands seemed not to confirm it, while the leukæmia developing, whether on a Mikulicz disease or not I cannot say, settled the matter.

Dr. W. F. Hamilton: I remember distinctly a case under my observation several years ago in which the spleen was greatly increased and the liver as well. A leucocyte count of 6,000 with a variety of cells corresponding to myelogenous spleno-leukæmia. The man was forty years of age. It was reported by me as a case of Leube's leukanæmia. I would like to ask if the leukanæmia is not a type distinct from leukæmia.

Dr. Horst Qertel: With regard to Dr. Hamilton's question I am quite willing to admit that my use of the term leukanæmia does not exactly correspond to what Leube originally described, because in his first case, to which he applied the term, there existed, as Dr. Hamilton has pointed out, a blood picture of a pernicious anæmia with only a moderate increase of leucocytes, but great relative increase of mononuclears. In this case, while the anæmia

was very grave, the blood picture was no strictly that of a pernicious anæmia and the white cell increase was distinctly leukæmia in quantity and quality. However, later reports have included in the group of leukanæmia all those profound blood alterations which show marked changes in the formation of red as well as white cells and in this sense, I believe, the term is applicable to this case.

PHOTOGRAPHIC DEMONSTRATION: By Dr. G. Gordon Campbell, showing a series of common skin diseases.

PAPER: The paper of the evening was read by Dr. E. H. Mason on the clinical application of functional diagnosis in nephritis.

DISCUSSION: Dr. C. F. Martin: I would like, first of all, to express my appreciation of the work Dr. Mason has put before the Society to-night. Having followed a good deal of this work for the past year or so, I have been able to see the exactness with which he has carried it out. A feature which interests us here to-night in connexion with this work is the demonstration that our older ideas about the anatomical and clinical classifications of kidney disease rather tend to be brushed aside. It is kidney *function* which gives the best idea of what the real state of the kidney is. I recall the frequency with which patients suddenly developed very serious kidney conditions when the ordinary tests that we adopted were negative, or almost negative. Pregnant women whose urine showed little or no evidence of albumin or other sign of disease, would no doubt by a functional test have given a different picture. We recognize pretty well that the mere presence of albumin in the urine and the mere taking of specific gravity once or twice amounts to nothing and tells little of what the kidney really can do. On the other hand we recognize that these tests can only be done with more or less training. Dr. Mason has told us to-night two facts: (1) that by simple measures we can estimate prognosis, and (2) that it is of great importance to study the nightly output from the kidneys and the decimal variations of the specific gravity. As to either the fallacy or correctness of Dr. Mason's observations it seems to me that the very constancy with which the results came out is sufficient to plead for their accuracy. The interesting fact that from day to day the observations that have been made have proved accurate, would go to show that evidently we have a great deal to look forward to in the usefulness of this test, and Dr. Mason is to be congratulated not only on the contents of his paper but on the way in which it has been delivered.

Dr. A. G. Morphy: One striking feature of this paper is the fact that the amount of the excretion of albumin by the kidneys in cases of nephritis is hardly mentioned. I would like to ask Dr. Mason whether he has been able to establish any relation between the amount of albumin excreted by the kidneys and the nitrogen tests which he employs. It really has a practical application. For instance, Dr. Mason says that in cases of passive congestion there is very little trouble with the excretion of urea, etc.; supposing he had a case of passive congestion with a leakage of albumin by the kidney, what practical application would that have upon the diet of the patient?

Dr. M. Lauterman: Dr. Mason's splendid paper recalls some work I undertook while a house surgeon at the Montreal Maternity Hospital some twenty odd years ago. He has established from proven facts theories which I then held, though unfortunately I was unable to go on with the work and prove my views. The first thing I would like to take issue on with Dr. Mason is the importance of the phthalein test: he states that the phthalein indication alone is of no value. As one who has done considerable surgery in connexion with the urological organs, I feel that this test alone is probably the best the surgeon has of his patient's ability to stand surgical interference. I do not mean to imply that the other valuable data to be acquired by the different tests Dr. Mason has outlined are not of value, I think they are probably of more value to the internist than to the surgeon, but in my opinion, and certainly from my experience, this phthalein test is the outstanding test of value as an index in surgical work. In my own limited experience I have classified these tests into two groups for my work, first the excretory, then the retention group. I believe with Dr. Mason that it requires a great deal of work and training and is beyond the average man, but that it is important is apparent not only to the average man but to every one of us who have heard this paper to-night and I am sure the development of this work will not only mark an epoch in this field but we shall be in a position to appreciate more fully the work that is being quietly done in our midst by careful and conscientious observers.

Dr. W. S. Morrow: I would like to express my personal appreciation of this paper to-night as this seems to me one of the subjects in which our knowledge has undergone a great deal of development lately and I would like to ask Dr. Mason, first, whether he often found any great amount of chlorine retention without its giving some clinical indication in the way of œdema,

and secondly, whether he found any serious degree of nitrogen retention without showing a drop in the total quantity.

Dr. E. H. Mason: As regards Dr. Morphy's question about the albumin I cannot say that I have found any relation at all between the function of the kidney and the amount of albumin in the urine. One might expect that those cases which have a large amount of albumin would show impaired urea excretion, but that is not so. A great many of our cases are purely chloride ones and have enormous amounts of albumin. If we cut down their protein intake there is the question whether the excretion of albumin would not decrease more rapidly than it would if we kept up a high proteid intake. But I have not found any relation between the various functions of the kidney and the amount of albumin excreted. As regards the dieting in passive congestion of the kidney, I think that the presence of albumin in the urine in passive congestion of the kidney would not to my mind make any difference at all as regards the diet. The fluid and the salt are the two things which need to be restricted, as these patients are often loaded up with fluid. I do not think the protein intake would influence the function to any appreciable extent unless a great deal was given. Epstein says that in chronic parenchymatous nephritis he does not cut down the protein intake at all; just the salt and fluid. As regards the question of the phthalein test, I spoke of this as of not much use alone, that is from the medical point of view; it is of value from the surgical. It is a test of the total kidney function, but it does not show whether the kidney can handle urea or chlorides. The phthalein is no index at all of what the disturbance is in the kidney, it just gives you the total kidney function, and from the surgical point of view that is the main thing. From the point of view of treatment it fails to tell anything as regards the necessity of cutting down the proteid, the salt, or the fluid in the diet. As regards Dr. Morrow's question, I think that in a general way you will find a disturbance of the chlorine metabolism associated with œdema. When you have œdema you almost always have a raised threshold which means damming back of salt within the body and most of the cases under our notice that have had chlorine retention have had œdema.

THE tenth regular meeting of the Society was held Friday, February 16th, 1917, Dr. W. S. Morrow, president, in the chair.

LIVING CASE: Glioma of the frontal lobe. The result of decompression, by Dr. G. S. Mundie.

The patient is a man of forty-four years, an overseer in a cotton mill. He was admitted to the Royal Victoria Hospital on November 6th, 1916, complaining of headache and attacks of hiccough. His illness began in March with headaches in the frontal region, in August he started vomiting, chiefly in the morning and of a projectile nature with no relation to food and no pain. Was in the Montreal General Hospital for seven weeks and there it was discovered that he had a marked optic neuritis on both sides. While there, he also developed incontinence of urine and fæces. The only other thing in the history is that one day while walking out he developed a paresis of his left leg, but this passed off in a short time. There was nothing in the family or personal history.

On admission to the Royal Victoria Hospital there was double optic neuritis with hæmorrhages into the retina; the other cranial nerves were negative. There was some indefinite involvement of the sensory system but nothing marked; no involvement of the motor system. The reflexes were increased on both sides, on the right more than on the left; there was incontinence of urine and fæces. There was a double ankle clonus, more marked on the right side; a questionable Babinski on the right side but definite on the left; no Oppenheim, no Gordon, no disturbance of joint sense. Slight incoördination of left side; on walking the patient has a tendency to fall to the right and backward. He would answer questions after two or three minutes and when asked to explain why he did not answer at once, he said he could not collect his thoughts.

On December 4th, the patient was in considerable distress, with marked pain in the head. Examination showed right ptosis, the right pupil dilated, active to light, and there was a slight lateral nystagmus. We were unable to get him to move the eyes; the left showed an external squint. Knee jerks increased on the right more than left; no Babinski on right side and a questionable on the left; there was a considerable paresis on the left side of the face. Another interesting thing was the fact that he had hallucinations, he definitely saw himself in a hippodrome in England and saw two Russians who were torturing him, and he went through other hallucinations. The question arose whether we had a cerebellar or a frontal lobe tumour to deal with. In his walking he deviated to the right, on the other hand he had this marked mental deterioration which pointed to a frontal lobe tumour. At first we were unable to decide on which side but what helped us eventually was the right ptosis and the left external squint. The man was gradu-

ally getting worse and we decided to operate. He was taken to the operating room and operated on in the right frontal lobe; the scar is quite marked here. The bone flap was turned down and there was marked tension of the brain which protruded at once. On opening the dura nothing but marked tension was noticed. The osteoplastic flap was turned down and the bone broken across. Dr. Archibald's report is as follows:

Brain very tense before dura opened, very slight pulsation. Posterior area uncovered was normal, but anteriorly the brain was congested and felt very soft; about one ounce of straw-coloured fluid was evacuated. A diagnosis of glioma was made and the dura was left open and the bone loosely replaced.

At first there was marked hernia, which has gradually disappeared and the man to-day says he is quite well. The bone is quite movable. The report when he was examined about a week ago showed: osteoplastic flap pushed out considerably so as to make right temporal region prominent; no bony union. General condition is very much improved; memory has improved so that his wife says it is normal; speech is normal and fluent, but patient is inclined to make jokes. Nystagmoid jerking on looking to right; paralysis of lower left facial muscles; tongue protruded slightly to left; left grip is much weaker than right. No incoördination, no weakness in legs. Reflexes are normal. Slight blurring of both optic discs, especially on nasal side, and a few comparatively recent retinal hæmorrhages.

The remarkable part of the story is the condition of the patient. He says he is practically well and able to go back to work. His memory has cleared up but on examination there is still slow cerebration, he does not execute demands as a normal person would.

The pathological report was, vascular cellular glioma.

The question arises here whether the decompression operation does any good or not and the case was presented to show that you do get more or less good results. As regards the future the outlook is not good but you have given the man anywhere from six months to a year of at least comfort.

PATHOLOGICAL SPECIMENS: Series by Dr. W. J. Scott.

1. Specimens from a case of acute pancreatic disease.

2. Specimen of heart showing numerous lacerations, though there had been no fracture of ribs, from a delirious patient who fell from a window to the street, four storeys below.

PAPER: "Fractures of the skull" was the subject taken up for

the paper of the evening. Dr. J. Anderson Springle discussed the subject from the surgical point of view while Dr. G. D. Robins took up the neurological aspect.

Discussion: Dr. A. E. Garrow: The Society is indeed indebted to the readers of these papers for a discussion on this very important subject, and more particularly for the list of aphorisms which Dr. Robins has referred to in the treatment of these acute conditions of the skull, to which I most heartily subscribe. I do not know that I am quite prepared to go the full length that Dr. Springle has gone for, as Dr. Robins has pointed out, there are really two types of cases which demand operative interference and decompression —at least operative interference in order to procure less pressure within the cranium. Those of epidural hæmorrhage due to rupture of the middle meningeal in which there is a gradually increasing engorgement of vessels certainly require decompression inasmuch as they require removal of bone and consequently removal of blood clot. Then those cases in which we have evidence of subdural hæmorrhage, as shown by blood in the cerebrospinal fluid with early evidence of concussion, with a certain amount of irritability and the gradual spread of œdema, are the cases in which some interference is called for. With opening of the dura in order to remove distension good results should follow. Whether it is good practice in every case of fracture of the skull, without some very definite evidence of compression, to be brought to the operating room and operated upon without very definite views as to what has happened in that brain, I am not quite prepared to say; one must hesitate before undertaking such very radical treatment.

Dr. F. R. England: I do not know that I can add anything to what has been said by Dr. Robins and Dr. Springle. In head injuries it is always an important question to decide whether the brain has suffered injury or whether the skull alone has been fractured. The cases referred to by Dr. Robins to illustrate a group of cases where there is no question as to the necessity of operative interference remind me of a case which was only recently admitted to my service in the Western Hospital. A young woman fell down stairs and showed symptoms of head injury. Three days later, when I first saw her, she was unconscious, pulse weak and soft, respiration slow, extremities cold, blood pressure 85, spinal fluid bloody. The whole picture was one of intracranial hæmorrhage where the end was fast approaching. The skull over the temporal region on the left side was opened and two ounces of

blood and clots escaped when the dura mater was incised from the middle fossa of the skull. A drainage tube was carried beneath the membranes deep down into the fossa and brought out through the angle of the scalp wound. All the symptoms rapidly improved; she was conscious next day and left the hospital in good condition at the end of three weeks after operation. Dr. Robins remarked that I held that the cases often did best where the injury had been very severe, where the skull had been shattered and driven down upon the brain with laceration of the membranes and even the destruction of the brain tissue. The recoveries in some of these cases is certainly rema kable, and they do not generally suffer from headache, mental feebleness, irritability, or traumatic neurasthenia so frequently seen following head injuries where no operative procedures have been carried out.

Dr. W. E. Archibald: Dr. Robins's paper has been extremely interesting. The question of whether one should operate or not in the presence of a fracture of the skull is in many instances one that taxes more the judgement of the surgeon, one that needs more careful and continuous scientific observation in its decision, than any other. There is, I find, a fairly large number of cases in which operation is obviously necessary; there are a certain number so severe that operation is either out of the question or is undertaken as a last resort and with practically no hope of doing the patient any good; and finally there remains a very large middle class of cases in which judgement as to operation is difficult. I have been tempted frequently to cut the Gordian knot of this difficulty by operating on all cases save the light ones, just as many of us do in the matter of appendicitis; that, however, is not a thoroughly scientific attitude. How are we to determine? It seems to me we have to take a panoramic view of all the symptoms; we must judge, not alone from a lumbar puncture, or alone from the blood pressure, but with these as compared with the work of the respiratory and the cardio-inhibitory centres, and with the depth of unconsciousness, and with the localizing signs which may be found in the examination of the nervous system. We must diagnose the pathological condition present within the skull-cap on the physiological basis. We must not think in terms of the text-book or the catalogue. In the presence of a slow pulse, one below 60, and unconsiousness, we all probably think that operation is strongly indicated; with disturbed rhythm of respiration we think it still more strongly indicated. But there are a great many cases in which blood pressure is not high, not over 150, in which the pulse

runs around 70 to 80, the respirations not at all disturbed, but consciousness is more or less lost: are we to operate on those? A great many of these will get well if you leave them alone, but some of them will die unexpectedly. I have come to see that in a certain number of cases you cannot tell by dint of taking the blood pressure, lumbar puncture, or observing the respirations, what they are going to do; and I have come to believe that in such cases the symptoms of compression, that is, high blood pressure and slow pulse, particularly, are masked by the symptoms of concussion, the low blood pressure and more rapid pulse, the result being that a happy medium or, if you will, an unhappy medium, is struck which leads one to a false sense of security. Therefore I am inclined more and more to concur in Dr. Springle's opinion that we should operate more frequently than we have been accustomed to do in the past. I have gone through stages, first, operating too often, second, too infrequently, and I have now come to the third stage where I operate more frequently than I did because many of these cases are apt to die suddenly without giving any sign that the graver condition was present.

Lumbar puncture is not of much value in the mere establishment of the fact that there is blood in the spinal canal; but it is of considerable value in showing how much blood there is. It is true that the more blood there is in the cerebro-spinal fluid the more serious is the condition present. On one occasion I found a lumbar puncture pressure of 1000 m.m. of water in a case of what was nothing more than concussion on the third day of the injury without rise of general blood pressure. This rise indicated an extreme degree of pressure in the cerebro-spinal system; I was able to relieve all his symptoms, particularly violent headache, by lumbar puncture alone. On the other hand you may get a very low lumbar puncture pressure when the brain stem is pushed down in the foramen magnum by serious intracranial compression, so that lumbar puncture by itself is of no great value in prognosis unless there is a large amount of blood in the fluid.

The idea that we can always relieve by decompression dangerous intracranial conditions needs, I think, modification. In a really bad case decompression will not save; in moderate cases it may perhaps save some, but will frequently be unnecessary as regards saving life. As to whether it is better to operate in order to forestall epilepsy, much has yet to be learned. I do not think myself that epilepsy is often staved off by decompression at the time of the accident. The late results of the head wounds in the

present war have shown that epilepsy has been surprisingly infrequent. Holmes and Sargent in 1100 cases of gunshot wounds of the cranium, examined six to eighteen months after the injury, found epilepsy and insanity to be remarkable by their absence.

Dr. G. D. Robins: I understand Dr. Archibald to refer to the number of cases that can be saved by operation in fracture of the skull as trifling; that is absolutely against our experience at the Western Hospital. There is no doubt at all in my mind that a large proportion of cases can be saved and have been saved by operation, that were clearly, from the way in which they were going on, certain to die otherwise. The case that Dr. England referred to is a notable illustration of this fact. As to what concussion means that is a disputed point, but I think it might be briefly defined as acute compression of the brain. I would like to refer to a case of fracture of the skull which I saw in the country, as representative not only of perfect recovery where there had been loss of cerebral tissue, but also as illustrating the great resistance to infection that the brain sometimes shows. A child three years of age went out behind a horse in a barn yard and was kicked in the frontal region close to the Rolandic area. I first supposed it was merely a torn scalp, but on examination I found the cerebral tissues freely mixed up with the hair and pieces of bone. The child was given an anæsthetic, the loose brain substance removed, and the brain cleansed as thoroughly as possible with peroxide of hydrogen. It was expected that meningitis would set in and the child die but he got better without an untoward symptom. A star case of Dr. England's at the Western Hospital may be mentioned. We have told of some cases that were very nearly dead and were saved by operation but we have not yet referred to the case that was actually dead (officially), and came to life again. This man was brought in with a depressed fracture of the frontal bone and in very bad condition. At operation the frontal bone was pried up, the hæmorrhage relieved and, contrary to all expectations, he recovered. In the meantime the newspapers had printed a report of the accident saying that the man had died, and subsequently the superintendent of the hospital, when called to the morgue regarding another case, found to his astonishment that an inquest was actually in progress on this man who was neither dead nor likely to die!

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